The Journal of Thoracic Surgery

VOL. 34 OCTOBER, 1957 NO. 4

Original Communications

THE USE OF RIGID PROSTHESES IN VASCULAR SURGERY

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THE USE of rigid vascular prostheses is, of course, not a new principle. Carrel,[1, 2] Blakemore,[3] Lam,[4] and others have employed them or considered their possibilities. It was not until Hufnagel[5-7] demonstrated that a nonwetting plastic, such as methyl methacrylate, could be tolerated for a long period, perhaps indefinitely, and remain patent that their use as vascular replacements became practical. The use of his ingenious multiple-point fixation principle permitted rapid placement and minimized the danger of vascular necrosis and slough.

The great advantage of the Hufnagel tubes (Fig. 1) is the rapidity with which vascular anastomoses can be performed. The necessity for speedy restoration of vascular continuity of the ascending aorta and of the carotid and renal vessels is obvious. We feel that time is a very important factor in resecting lesions of the descending aorta as well. The time factor in vascular anastomosis can be divided into two components. The first is the total operating time and the second is the duration of vascular occlusion. It seems apparent that an operation requiring only 3 hours, all other factors being equal, will have a lower mortality rate than an operation lasting 7 or 10 hours.

Studies which we are making with a flowmeter (Fig. 2) inserted in the descending aorta, and which will be reported elsewhere, have demonstrated that fall in the cardiac output is directly proportional to the length of the operation (Fig. 3). This is true under hypothermia as well, and a drop in cardiac

Read at the Thirty-seventh Annual Meeting of The American Association for Thoracic Surgery at Chicago, Ill., May 4-7, 1957.

Aided by grants from the San Diego and Los Angeles Heart Associations and Stanley Kramer.

output due to decreased tissue metabolism is tolerated only to a certain point, the coronary flow required being disproportionate to the needs of the remaining body tissues. When the descending aorta in dogs is clamped for varying periods of time (Fig. 4), further flowmeter studies reveal that after about 20 minutes, the cardiac output is very slow to recover and, during the duration of the acute experiments, never recovers completely to the original reference point. It is true that output gradually rises during the postoperative period but in a poor-risk patient this factor may represent the difference between success and failure of the procedure.

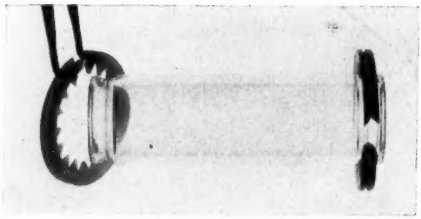


Fig. 1.—The straight Hufnagel tube with multiple-point fixation rings.

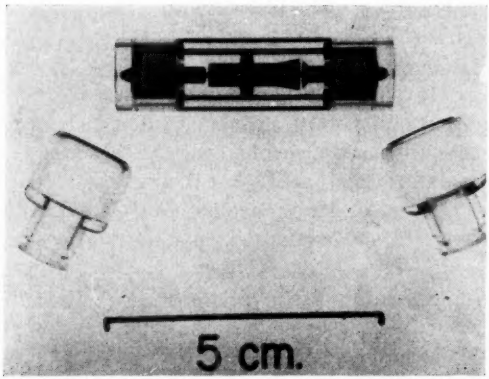


Fig. 2.—Turbine-type flowmeter with plastic couplers for aortic insertion.

To a considerable extent, the problem of prolonged vascular occlusion can be solved by the use of by-pass shunts, either direct or through a pump system. There are certain disadvantages of such shunts, however. The direct by-pass shunt requires at least two anastomoses in addition to the principal lines of anastomosis and each suture line requires at least ½ hour and usually more, thus adding to the total operating time. In by-passing the smaller vessels, it is difficult and sometimes impossible to place a partial occluding clamp in such a way as to leave an adequate cuff without causing total occlusion. The pump method of shunting has the problems associated with all pumping systems.

Recognizing this need for rapid anastomosis Freyfogel,[8] Schafer and Hardin,[9] Izant,[10] Kelly and Alden,[11] and de Villegas[12] and their co-workers

have devised quite ingenious methods of accomplishing this. The methods that we wish to present provide an additional means of attaining this goal. It is not intended that they replace the conventional methods of vascular suture, but it is hoped that they may occasionally serve as an adjunct.

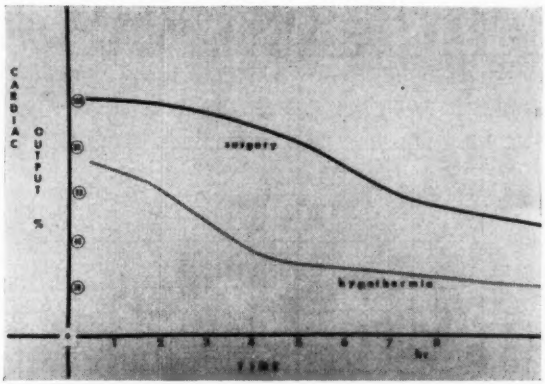


Fig. 3.—Cardiac output as measured by the aortic flowmeter during open chest operation under normothermia and hypothermia.

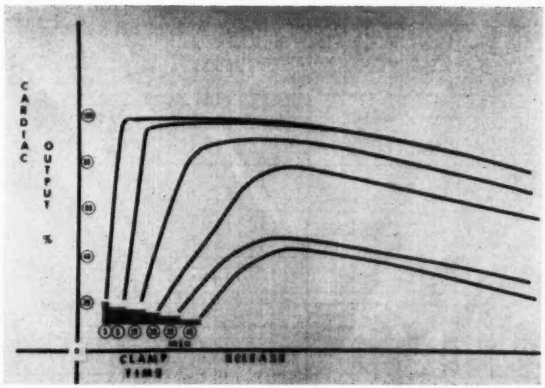


Fig. 4.—Cardiac output determinations after varying durations of descending aorta cross-clamping. The critical point in dogs appears to be about 20 minutes.

During the past 3 years, we have employed Hufnagel type tubes and modifications of them in the experimental laboratory and during this time various methods of utilization have suggested themselves.

METHODS OF UTILIZATION

I. As simple replacement.
   a. Straight.
   b. Branched.
   c. Arch.

II. As rigid couplers with other conduits.

III. As internal shunts.

a. Temporary with homograft or cloth.

b. Permanent through an aneurysm.

IV. As a method of restoring single channel flow in dissecting aneurysm.

In simple replacement, as described by Hufnagel, substitution for a segment of vessel by a straight tube can be accomplished within a few minutes (Fig. 5). In the animals sacrificed after 3 years the tube was encased in fibrous tissue. The external appearance suggested continuity of the aorta and the

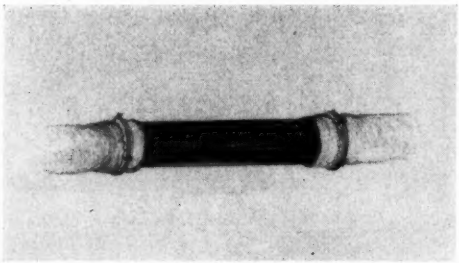


Fig. 5.—Simple replacement of aortic segment with Hufnagel tube. This is usually accomplished in 3 to 7 minutes.

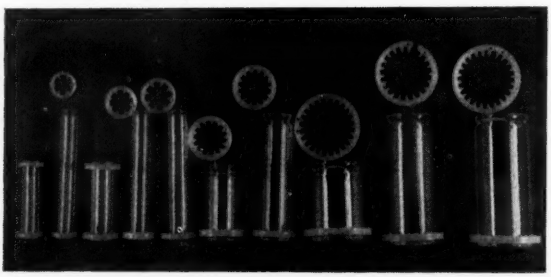


Fig. 6.—Hufnagel tubes are available in a variety of calibers and lengths.

interior of the tubes showed no evidence of clotting or endothelial proliferation. These tubes are presently available in a range of length and calibers from The Brunswick Co. (Fig. 6). Special tubes can be made which are tapered to accommodate disproportion of the vessel ends (Fig. 7).

Tubes with branches can be fashioned and replacement of the segment of aorta bearing the renal arteries is being investigated (Fig. 8). By providing brachiocephalic branches, it has been possible to replace the aortic arch in dogs within a period of less than 5 minutes with good recovery (Figs. 9,*A* and 9,*B*).

When the rigid tubes are used as couplers, other types of conduits such as nylon and Dacron sleeves and Edwards-Tapp arterial tubes may be quickly inserted (Fig. 10). The need for flexibility obviously limits the length of the simple replacement tubes. This method proved useful in a clinical case when one of us (J. F.) was called in consultation because it had not been possible to obtain

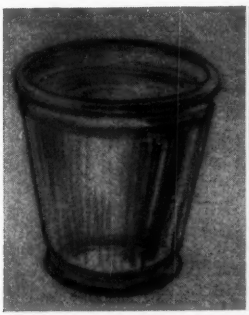


Fig. 7.

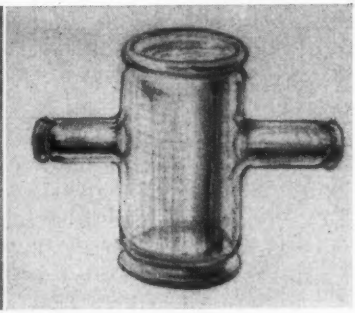
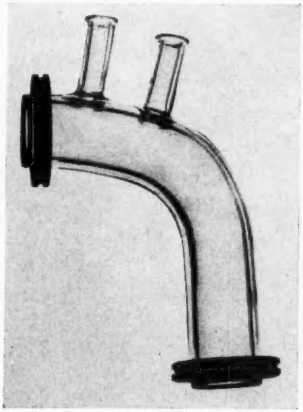


Fig. 8.

Fig. 7.—Tapered tube to accommodate disproportion of vessel ends.
Fig. 8.—Branched tube suitable to be used as a coupler for abdominal aneurysms involving renal arteries.



A.

B.

Fig. 9.—*A*, Canine aortic arch prosthesis. *B*, Canine aortic arch installed in 5 minutes with complete recovery of animal.

a tight proximal suture line, in numerous attempts, after excision of an abdominal aneurysm, because of disproportion and extreme friability of the proximal aorta. The use of a ring and coupler solved the problem and the patient made a good recovery.

Another clinical case in which a coupler was employed was in an aneurysm of the aortic arch. A 69-year-old man was admitted to Wadsworth Veterans'

Hospital complaining of chest pain, weight loss, and marked fatigue. Roentgenograms of the chest (Figs. 11*A* and 11*B*) revealed a large aneurysm involving the aortic arch. Resection of the lesion appeared advisable and a homograft replacement with multiple by-pass shunts was contemplated. However, his blood pressure fell quite precipitiously on opening the chest and could not be restored. It seemed apparent that he would not tolerate the prolonged procedure necessary to place a homograft and the chest was closed. Following recovery from the anterior bilateral second interspace thoracotomy, his pain became more severe, he began to have hemoptyses, and left recurrent laryngeal nerve paralysis occurred. Two weeks following the original operation on Oct. 24, 1956, the chest was re-opened through the old incision. Exploration revealed the aneurysm shown in Fig. 12,*A*. A partial occluding clamp was placed on the ascending aorta and a large caliber Edwards-Tapp tube was sutured end-to-side (Fig. 12,*B*). On the distal end of the tube a coupler had been wired in place. The aorta was then doubly clamped distal to the aneurysm and

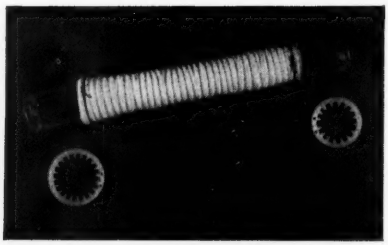


Fig. 10.—Rigid tubes used as couplers for a cloth conduit, in this case an Edwards tube. Cloth sleeves and homograft segments have also been used.

the coupler inserted distally and secured by a multiple fixation ring (Fig. 12, *C*). The distal clamp was then removed, after a total occlusion time of 7 minutes, permitting flow through the shunt. A nonerushing clamp was then placed in such a manner as to exclude the aneurysm but preserve the carotid arteries. The aneurysm was then excised, the proximal end being closed with a continuous mattress suture and a continuous over-and-over suture (Fig. 12,*D*). Recovery was essentially uneventful and he is asymptomatic, save for hoarseness, 6 months after operation. (Figs. 13*A* and 13*B*.)

It has been our experience that the superior aspect of the aortic arch is often not involved in the aneurysmal process and it seems feasible in some instances to tailor the aorta in such a manner as to preserve these vessels in continuity, as described by Bahnson.[13]

These prostheses have also been of value as internal shunts during anastomosis. A segment of homograft or cloth tube is slipped over a tube of appropriate length (Fig. 14). The aorta is then cross-clamped and the lesion excised. The prosthesis is then fixed in each end with the rings, the ring-holders being left in place as handles. The aortic clamps are then removed, restoring flow. The usual occlusion time is 3 to 7 minutes. The homograft or cloth can now be straightened out and the suture lines made. The aorta is easily rotated

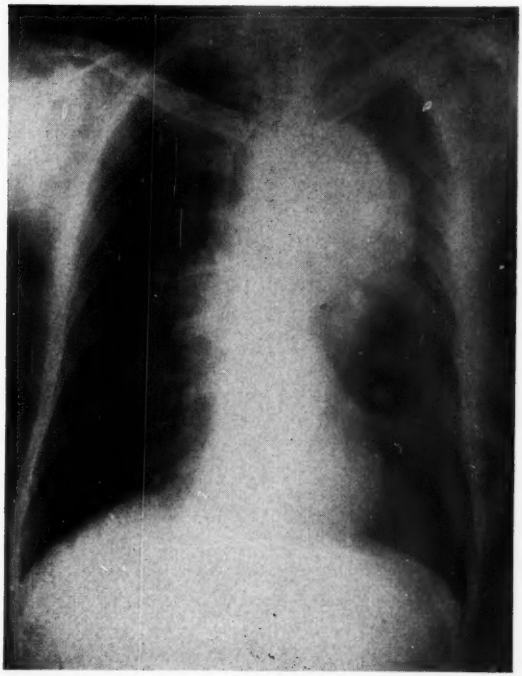


Fig. 11*A*.—Chest x-ray of 69-year-old man with aneurysm of arch.

Fig. 11*B*.—Retrograde aortogram of same case.

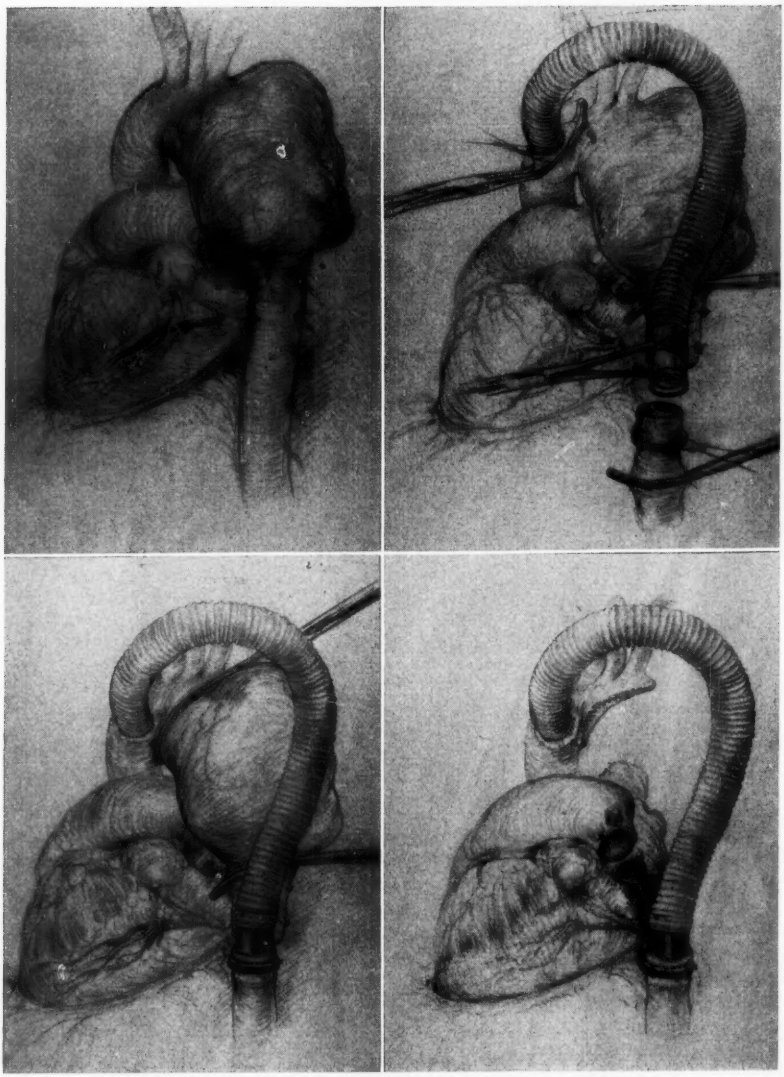


Fig. 12.—*A*, The aneurysm observed in Figs. 11*A* and 11*B*.

B, End-to-side anastamosis between ascending aorta and Edwards tube. Rigid coupler being inserted in descending aorta which has been cross-clamped.

C, Coupler in place and distal aortic clamp removed. Total occlusion time was 7 minutes.

D, The aneurysm has been excised contouring the excision to preserve superior aspect of arch. Total operating time was 3½ hours.

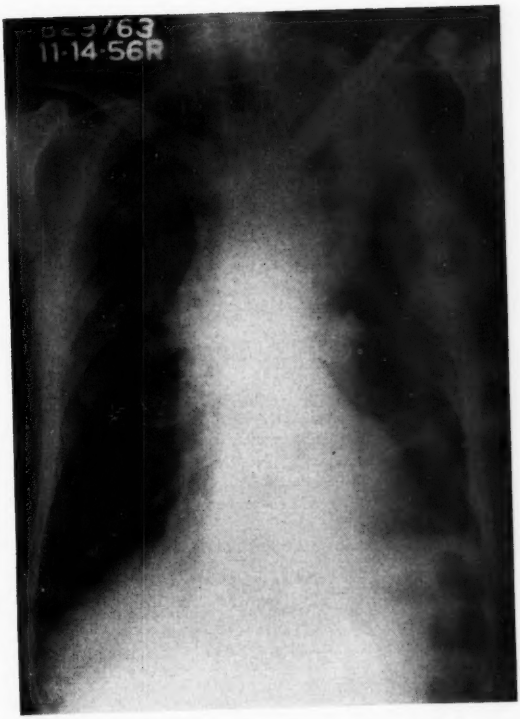


Fig. 13*A*.—Chest x-ray 6 weeks postoperatively.

Fig. 13*B*.—Postoperative retrograde aortogram.

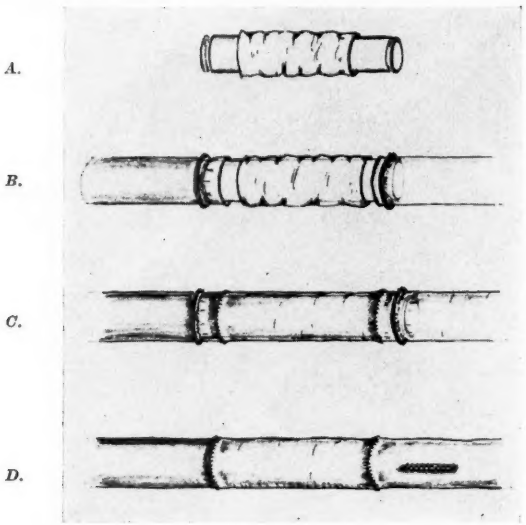
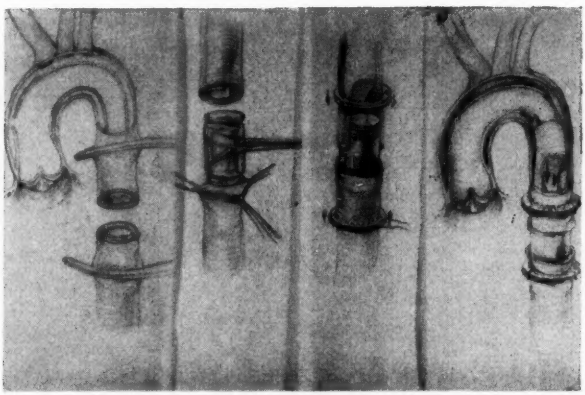


Fig. 14.—*A*, Segment of homograft slipped over a rigid tube.

B, The aorta has been cross-clamped and tube installed.

C, The graft is straightened and sutured in place. The aorta can be rotated to complete posterior suture line.

D, The rings have been removed with the aorta cross-clamped above and below and the prosthesis slipped out through a longitudinal incision. The small incision was closed with a partial occluding clamp and the cross-clamps removed. The incision has been sutured over the partial occluding clamp.



A. *B.* *C.* *D.*

Fig. 15.—*A*, The dissecting aorta has been cross-clamped and divided.

B, A portion of the partition above has been excised.

C, The prosthesis has been placed in the single channel above and the true channel below.

D, The redirected flow into the true channel. If desired the aortic ends may be closely approximated and a suture anastomosis made. The prosthesis can then be removed as described previously.

with the ring holders to permit access to its undersurface. The aortic clamps are then re-applied, the fixation rings are removed, and the prosthesis delivered through a longitudinal incision above or below the grafted segment. A partial occluding clamp is applied to this incision and the cross-clamps are removed. This period of occlusion is usually 3 to 5 minutes.

In the treatment of dissecting aneurysms, it is also possible to apply this principle. The descending aorta is cross-clamped and transected. A portion of the partition above is excised as performed by DeBakey[14] and the tube placed and fixed in the single lumen created above and the true channel below. The cross-clamps are then removed. The prosthesis can be left in place or the aortic ends sutured together and the prosthesis removed as described previously (Fig. 15,*A, B, C, D*). This method was successfully employed in the case of a 35-year-old veteran. He has had no difficulty in the 2½ years since operation.

SUMMARY

Experimental and clinical studies of rigid plastic prostheses suggest that the methods described warrant consideration in certain instances when rapid restoration of flow is desired. These methods are not intended to replace conventional methods of vascular anastomosis, but it is hoped that they may be a useful adjunct.

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DISCUSSION

DR. IRVING A. SAROT, New York, N. Y.—I have enjoyed, as I am sure you all have, this excellent presentation by Dr. Byron. I should like to present a case in which an aortic homograft was placed as a permanent by-pass before resection of the aneurysm.

This eliminated the need for cross-clamping the aorta, temporary by-pass shunts or other temporary by-pass procedures. This patient was operated upon in October, 1954, and reported in 1955 (Sarot, I. A., and Lazzarini, A.: Resection of Aneurysm of the Aortic Arch and Descending Aorta: Permanent "Bypass" Homograft, Trans. Am. Coll. Cardiology 5: 175A-175N, 1955), so that this is a follow-up report.

When this 38-year-old woman presented herself in 1954, there had been as yet very little reported experience with temporary or permanent by-pass shunts. Albanese and Lazzarini had successfully treated a coarctation of the abdominal aorta, from below the coeliac trunk to just above the renal arteries, by placement of an aortic homograft as a permanent by-pass before resection of the coarctation. Mahorner and Spencer had done a two-stage procedure with a permanent by-pass homograft for an innominate artery aneurysm. But we found no reports of the use of such permanent by-pass homografts in the region of the aortic arch or the thoracic aorta.

The patient had been referred for treatment of a mediastinal tumor which had been causing cough and pain in the upper left back. She had been severely injured and in shock for several days following an automobile accident 14 years previously. Although a haziness at the left lung root had been seen on the roentgen film of the chest, at that time aortic injury had not been suspected.

(slide) Angiocardiography revealed a fusiform and sacculated aneurysm of the distal aortic arch and proximal descending thoracic aorta. This region is commonly the site of traumatic aneurysm following laceration of the aorta due to the rapid deceleration in automobile accidents.

(slide) At operation, the aneurysm was found to involve the origin of the left subclavian artery as well.

(slide) An aortic homograft was placed from the mid-portion of the aortic arch to the descending thoracic aorta by-passing the aneurysm.

(slide) The aneurysm was resected after the circulation was carried by the permanently placed by-pass homograft. At no time was the aorta cross-clamped or occluded. The sutured proximal end of the aortic arch, the adjacent left common carotid artery and the ligated distal end of the left subclavian artery are visible. The proximal part of the latter artery was resected with the aneurysm. The distal stump of the aorta was left somewhat long, as can be seen here and, at an earlier presentation of this case, critical opinion was expressed that this somewhat long stump might cause trouble later. It was also suggested that the sudden change in the direction of the flow might cause degenerative changes in the homograft. However, nothing untoward seems to have occurred during the past 2½ years.

(slide) The resected aneurysm is shown after having been opened. The abrupt end of the normal aorta into the sacculation seems characteristic of complete transverse lacerations at this site following rapid deceleration in automobile accidents.

The patient recovered rapidly and pulses were present in all four extremities, including the left arm and wrist. She had a temporary hypertension of moderate degree but otherwise did well.

(slide) Angiocardiogram 3 months later revealed a well-functioning shunt. It is now more than 2½ years since operation and chest films (slide) show no evidence of unusual calcifications or other abnormalities in the region of the graft. The patient is well and working full time as a saleslady, on her feet many hours each day. She has a normal blood pressure and is asymptomatic. Unfortunately, I have not been able to induce her to have another angiocardiogram.

The simple procedure of placing a permanent by-pass homograft eliminated the necessity for complicated apparatus and procedures. I believe that it is a method which merits further consideration.

DR. RALPH A. DETERLING, JR., New York, N. Y.—We have had a great interest in the by-pass technique also, but mainly in peripheral occlusive disease. However, we

have had 2 patients in whom a by-pass was very suitable in the thoracic aorta. One was a lady, aged 47, with a long coarctation just above the diaphragm, whose right lung had essentially no ventilatory capacity. We were able to operate but not to compress the lung very much. It was very simple to insert a by-pass homograft behind the lung into the aorta above and below the stenosis and to restore normal blood pressure. Our second case was similar to that of Dr. Sarot; a man with a posterior right arch who had developed an aneurysm. We excised it and used a permanent by-pass homograft as described by Dr. Sarot. Unfortunately our man died at the end of the week of causes unrelated to the graft. I agree that this technique certainly merits a considerable bit of attention. Excision of thoracic aneurysms can be a very dangerous operation. In selected cases, the use of a permanent by-pass with excision of the lesion is far simpler than use of hypothermia or partial perfusion (controlled extracorporeal circulation.) I believe that the literature shows that Dr. Adams used a by-pass for thoracic aneurysm prior to the case Dr. Sarot has reported.

DR. MAX G. CARTER, New Haven, Conn.—I should like to ask a question of Dr. Byron and his colleagues. Everyone here, I am sure, has been aware that following insertion of a Hufnagel valve, there is danger of proximal aneurysmal dilatation and thrombosis because of the rigid ring inserted in the vessel. To prevent this, Dr. Hufnagel wraps both ends of his prosthesis with one of the synthetic cloth materials. I suppose this hazard is much greater in a patient with aortic insufficiency because of the wide excursion of the aorta. I would like to ask Dr. Byron if, in these multiple applications, this problem has been common. Further, since there may be some angulation where the by-pass grafts are put in rather obliquely, has this caused any erosion or aneurysmal dilatation at either end?

This is an excellent presentation and I enjoyed it very much.

DR. M. E. DEBAKEY, Houston, Texas.—I too enjoyed this presentation and I am sure there are some circumstances where it would be very desirable to use this prosthesis. Our own experiences with aneurysms of the thoracic aorta have led us, however, in a little different direction in overcoming some of the problems of temporary occlusion of the aorta for aneurysmal resection. In our experience, the type and location of the aneurysms we have encountered are such that this type of prosthetic device in facilitating the suture of the anastomosis would be virtually impossible. By that I mean that there is frequently and, in fact, in most instances, an inadequate margin of the aorta available to permit insertion of a temporary prosthesis for this purpose. Indeed, the margin is usually only enough to allow placement of the sutures for the anastomosis. The problem, we find, is often one, too, in which insertion of the prosthesis may actually add to the complexity of the operation. However, attempts to find ways and means of facilitating this procedure are certainly desirable, and I want to congratulate the authors on their efforts to achieve this objective.

DR. F. X. BYRON, Beverly Hills, Calif. (Closing).—I would first like to thank Dr. Sarot and Dr. Deterling for their interesting case presentations. So far as Dr. Carter's question is concerned, as to aneurysm formation, we have not found this to occur. Our series of Hufnagel valve operations is small, comprising some 20 odd cases, but we have not had aneurysm formation in any of these. I realize that it is a real hazard, but it is one that we have not as yet encountered.

With regard to Dr. DeBakey's remarks, I am thoroughly in agreement with him, and the situation has to be evaluated thoroughly at the time of operation. I will grant that in the majority of instances the conventional method of grafting is preferable, but there are occasional cases in which this might facilitate the procedure and therefore it might prove useful.

DIAGNOSTIC AND PHYSIOLOGIC MEASUREMENTS USING LEFT HEART CATHETERIZATION

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THREE years ago, a new technique for catheterization of the left side of the heart was described.[1] Since that time, the original technique has been modified[2] and new procedures have been added[3] in order to permit a more precise diagnosis and evaluation of patients with mitral and aortic valvular disease[4] in whom no definitive diagnosis could be obtained by the usual clinical studies. With a more accurate preoperative anatomic diagnosis, the operative mortality should be decreased in severely ill patients or in those who have multivalvular lesions by better selection of the patients who shall be operated upon and by choosing the best operative procedure. With this technique of left heart catheterization, it is possible to measure simultaneous left heart and aortic pressures and, by calculation, to estimate the left atrial, ventricular and aortic mixing volumes, and forward and regurgitant blood flows. These data can be used to provide information concerning the type and functional severity of valvular lesions; the left atrial, ventricular, and aortic volume abnormalities; the characteristics of the blood flow in the left heart chambers; the mechanisms of production of heart sounds, including gallop rhythm; and estimates of ventricular work and rates of ejection of blood from the left ventricle. Several methods have been reported for gaining access to the intracardiac chambers of the left heart. These include left atrial puncture by way of the bronchoscope,[5, 6] by a right paravertebral approach,[7] or by a suprasternal approach,[8, 9] as well as direct puncture through the ventricle[10, 11] and retrograde catheterization.[12, 13] Among the foremost contributors to these techniques have been Fisher,[14] Wood and his associates,[15] and Morrow[16] in this country, Björk and his co-workers in Sweden,[1, 7] and Allison[6] and Brock[11] and their associates in England. This paper presents our experience with 51 patients who have had catheterization of the left heart.

From the Harrison Department of Surgical Research and the Edward B. Robinette Foundation, and the Medical Clinic of the Hospital and School of Medicine of the University of Pennsylvania, Philadelphia, Pa.

This work has been supported by Grant No. H-393-C7, the Southeastern Pennsylvania Heart Association and the Atomic Energy Commission.

Read at the Thirty-seventh Annual Meeting of the American Association for Thoracic Surgery, Chicago, Ill., May 4-7, 1957.

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PROCEDURE

Patients with clinical evidence of mitral and aortic valvular disease are first evaluated by the usual clinical and laboratory studies. These include history and physical examination, electrocardiogram, fluoroscopic examination, and angiocardiography and "right-heart" catheterization when indicated.[17, 18] If the diagnosis remains in doubt following these studies the patient is considered for catheterization of the left side of the heart.

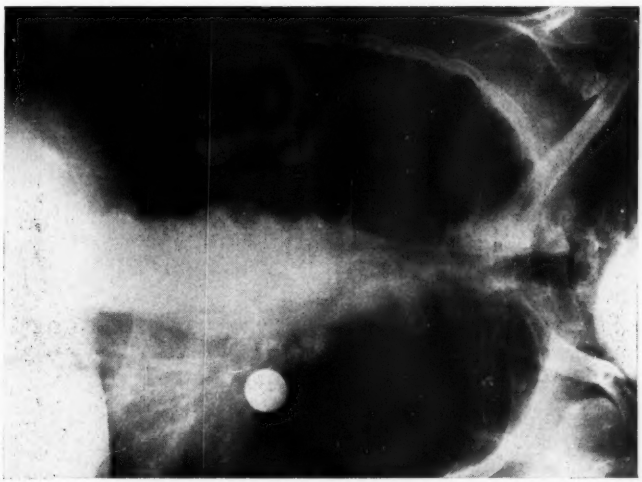


Fig. 1.—A roentgenogram of the chest taken, with patient in the left lateral decubitus position, for the purpose of determining the position of the left atrium. Markers are placed 5 cm. lateral to the dorsal spine over the right seventh and ninth ribs and the left eighth rib.

A study of the blood coagulation mechanism* is then performed, and corrective therapy given when indicated. If correction of the coagulation defect is not possible, the risk of the procedure is again assessed before proceeding. A roentgenogram of the chest is taken with the patient placed in the left lateral decubitus position. Coins are placed over the eighth rib on the left side and the seventh and ninth ribs on the right side, 5 cm. lateral to the spinous process (Fig. 1). The size and position of the left atrium with relation to the overlying rib are thus obtained. The patient who has been fasting for 6 to 12 hours is given a barbiturate (secobarbital 0.1 Gm.) and 300,000 units of penicillin intramuscularly 45 minutes prior to the study. Via a thin-walled No. 19 needle inserted percutaneously into the left femoral artery, a flexible 90 cm. polyvinyl radiopaque catheter is passed under fluoroscopic guidance into the ascending aorta.[19]† A slight curve is made in the end of the catheter before inserting it into the needle. This has been found to be helpful in passing the catheter around the arch of the aorta. The needle is

*We are indebted to Dr. Harold Wurtzel for the coagulation studies.

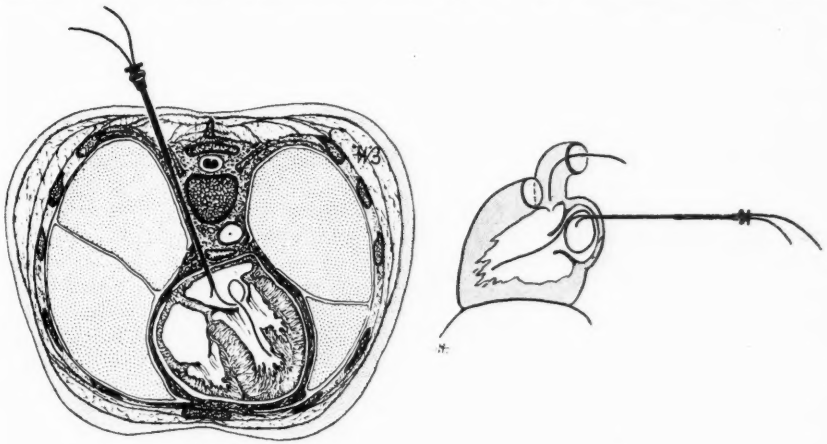
†Catheters for these procedures have been made by Mr. Albert Afford, Department of Physiology, School of Medicine, University of Pennsylvania.

then withdrawn over the catheter and digital pressure applied to the site of the puncture for a period of 5 minutes. Patency of the catheter is maintained by a constant drip of a dilute solution of heparin in saline. A site for sampling blood and for obtaining isotope-dilution curves is provided by placing an indwelling Cournand needle in the right brachial or femoral artery. The patient is then turned to the left lateral decubitus position. If the patient is dyspneic in this position, the head of the table may be tilted 10 to 15 degrees upward. The coins are removed and the skin prepared with an antiseptic solution. One per cent procaine solution is injected into the skin, 5 to 7 cm. to the right of the spinous process judged, on the basis of previous x-ray studies, to be nearest the center of the left atrium. The distance from the spinous process will vary with the body habitus of the patient. A 20 cm. thin-walled needle with a 1 mm. internal diameter* is passed paravertebrally over the eighth or ninth rib, using additional procaine when the pleura is punctured. As the body of the vertebra is passed, the stylette is removed and a negative pressure is applied to the needle by a syringe filled with 0.9 per cent saline solution. Increased resistance is usually encountered as the left atrium is punctured. Since, anatomically, most of the posterior aspect of the heart is made up of the left atrium, this chamber can be entered first if the heart is approached at the proper angle. The optimal site of puncture is probably that portion of the left atrium lying between the pulmonary veins where there is minimal movement with atrial contractions and the wall is less likely to tear. When the needle tip has entered the left atrial cavity, oxygenated blood can be aspirated and left atrial pressures recorded. The tip of the needle is then advanced an additional 0.5 to 1 cm. with care being taken that the tip does not pass through the interatrial septum into the right atrial cavity or through the left atrial wall into the root of the aorta. A small polyvinyl catheter† is passed into the atrium and manipulated until its tip lies within the left ventricle (Fig. 2, *A* and *B*). A second catheter is passed through the same needle into the atrium. Pressure measurements and radiopotassium (K^{42}) isotope-dilution curves are then obtained in the following manner. Pulse pressure recordings are made with 3 Lilly capacitance manometers coupled to a 5-channel oscillograph, a 2-channel direct writing Brush recorder, and a 2-channel oscilloscope. With this system, simultaneous recordings of left atrial, left ventricular, and aortic pressures are made, via the three small catheters previously introduced. Simultaneously, one lead of the electrocardiogram is recorded and, in most instances, phonocardiographic records are also obtained. (In addition, visual monitoring of the ECG and pulse pressure curves is carried out during the entire procedure.) The mid-dorsal line is used as the zero point of reference for the pressure determinations. The type of record obtained is demonstrated in Fig. 3. Following the pressure measurements, consecutive "instantaneous" injections of 15 to 20 microcuries of K^{42} in a volume of approximately 0.2 ml. are made into

*Manufactured by Stille, Stockholm, Sweden.

†Catheters for these procedures have been made by Mr. Albert Afford, Department of Physiology, School of Medicine, University of Pennsylvania.

the left atrium, left ventricle, and root of the aorta. After each injection, arterial blood samples are taken from the femoral or brachial artery for a period of 30 seconds and passed through a scintillation counter connected to a logarithmic counting rate meter and a recording system. The log of the arterial radioactive potassium concentration is recorded with respect



A. *B.*

Fig. 2.— *A*, Schematic transverse section through the chest showing course of the needle in right paravertebral puncture of the left atrium. Two small catheters are threaded through the same needle and one is manipulated into the left ventricle.

B, Sagittal section through heart demonstrating site of left atrial puncture and course of the catheters within the left side of the heart. Also indicated is an additional catheter which is passed via a percutaneous puncture of the femoral artery into the ascending aorta.

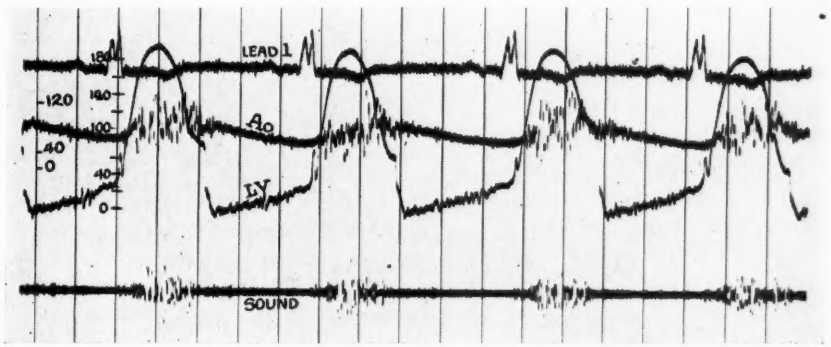


Fig. 3.—Photographic record taken during study of a patient with aortic stenosis. From top to bottom, respectively, are Lead I of the electrocardiogram, aortic pressure tracing (*Ao*), left ventricular pressure tracing (*LV*) and sound tracing recorded at apex of the heart.

to time in each case, giving three isotope-dilution curves. In addition, an attempt to quantitate the amount of mitral insufficiency is made by sampling the left atrial blood as well as femoral arterial blood following the injection of K^{42} into the left ventricular cavity. For this study, a different No. 18 thin-wall

needle* is used initially for the left atrial puncture (Fig. 4). It has a double attachment at the base and pressures can be measured via the single catheter from the left ventricle or around the catheter via the side arm from the left atrium. Left atrial blood is sampled via the side arm following injection into the left atrium of radioactive potassium. Not only can the regurgitation of the radioactive material into the atrium be detected but, also, the atrial dilution curve area can be related to the peripheral arterial dilution curve area so as to permit estimation of the actual amount of mitral regurgitation. Finally, the pressure measurements are repeated and the catheter within the ventricle is then slowly withdrawn into the atrium and the changes in pressures are recorded.

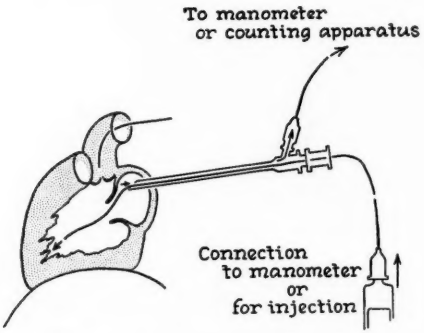


Fig. 4.—Schematic sagittal section through the heart showing optional No. 18 thin-wall 20-cm. needle used for puncturing the left atrium. A single catheter can be manipulated into the left ventricle and pressures can be measured or radioisotope injected into the left atrium and atrial pressures and/or blood samples can be obtained via the needle and side arm.

Major complications following this procedure are few but may be dangerous. It therefore seems advisable to perform the study only when an experienced thoracic surgeon is immediately available. The major complication which we have encountered has been that of bleeding. In 2 patients, cardiac tamponade resulted from bleeding into the pericardium. One of the patients had an immediate thoracotomy and is the only death in this series of 51 patients. The second patient with cardiac tamponade was successfully treated by pericardial aspiration on two occasions. This patient had aortic stenosis and, as is usually encountered with this lesion, the left atrium was small in relation to total cardiac size. Despite efforts to avoid direct puncture of the left ventricle from this approach, it is believed that the ventricle and perhaps one of the coronary vessels were punctured in this patient. In 4 additional patients, a decrease in hemoglobin concentration was considered to be of sufficient degree to warrant transfusions as a precautionary measure. In these patients the site of blood loss was not clearly ascertained. Serious infections have not been noted but 4 patients have had fever following this procedure. In 2 of these patients, leukocytosis was not noted and the fever may have

*Needle from Becton, Dickinson and Company.

been due to an unrelated infectious process that was seen at the same time in other patients on the hospital ward. The complication of air embolism has not been recognized and the hazard of air embolism is probably small because, in most patients with mitral stenosis, the left atrial pressure is positive throughout all phases of the cardiac cycle. In other patients, however, left atrial pressures may be negative during part of the cycle and care should be taken to prevent entrance of air into the left atrium. The problem of gaining access to the left atrial or left ventricular cavities has arisen on 9 occasions. In 3 patients, the left atrium could not be entered with the patient in the lateral decubitus position. In one of these where the difficulty was apparently due to a marked scoliosis with the concave curvature of the spine to the right, the needle was introduced into the right atrium and into the pulmonary artery. Proper puncture was subsequently accomplished in all 3 cases when the patient was placed in the prone position as used by Fisher[14] and others.[13] In 6 patients, the catheter could not be manipulated from the left atrium into the left ventricle. The difficulty was overcome by the use of catheters which were less stiff than those previously used but less pliable than polyethylene catheters which have been reported to have formed knots in the heart.[20] Severance of the catheter at the needle tip while the needle is still within the heart has so far been avoided. This may be due to the practice of two precautionary measures: (1) the use of a needle having its bevel blunted at the base, and (2) removal of the needle and catheter together if the catheter cannot be withdrawn easily through the lumen of the needle.

TREATMENT OF DATA

The atrial, ventricular, and aortic pressure curves are replotted so that they are superimposed using a single pressure scale in the proper time relationships (Fig. 5). The mean aortic and mitral transvalvular pressure gradients and the instantaneous gradients (particularly the largest and the end-diastolic in the case of the mitral valve) are then obtained. From the K^{42} dilution curves, cardiac output, regurgitant blood flow, if present, and left atrial, left ventricular and aortic mixing and total volumes are calculated.[3, 21] Left ventricular work can be calculated using the appropriate pressure and flow values. The mean pressure gradient and the blood flow across the valve under study are inserted into the proper hydraulic orifice flow formula and valve orifice area is calculated.[22]

When the phonocardiographic tracing is also obtained, it is aligned with the replotted pressure and time data and the electrocardiogram as described elsewhere,[23] so that the sounds may be correlated with changes in the pressure gradients and electrical events occurring during a cardiac cycle. Since the stroke volume and instantaneous pressure gradients across the aortic valve are available, it is possible, assuming that the flow across the valve is turbulent, to estimate left ventricular ejection volume during any part of ventricular systole. That is, the ejection volume at any time should be related to the square root of the gradient across the valve at that time. Therefore,

when the stroke volume and the instantaneous gradient and their sum are known, the ejection rate can be calculated. Further investigation will be required before this hypothesis can be fully tested and its usefulness determined particularly in the evaluation of ventricular work.

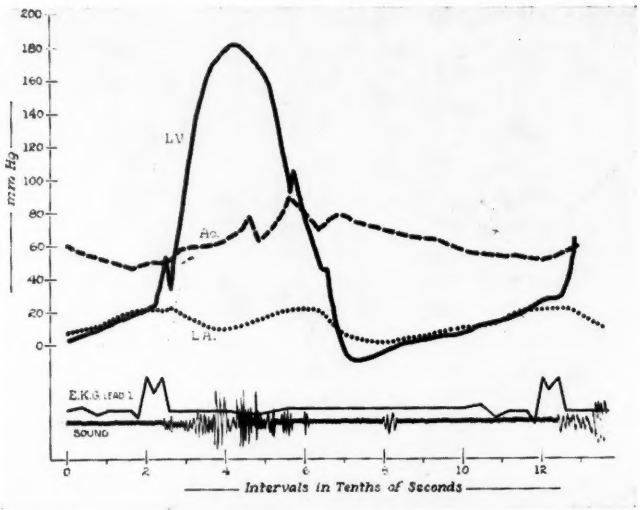
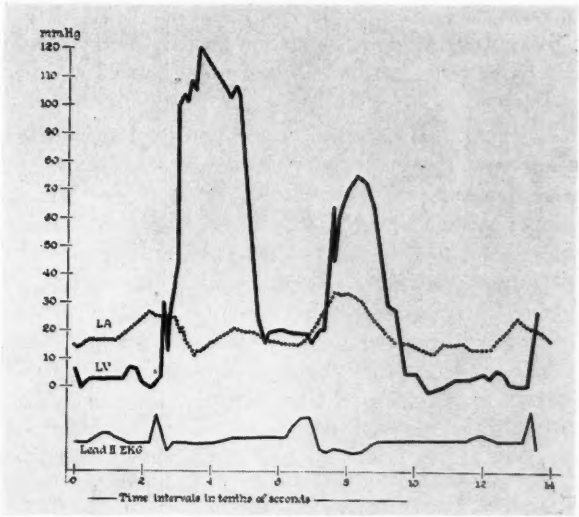


Fig. 5.—Recording of left ventricular (*LV*), aortic (*Ao*), and left atrial (*LA*) pressures, ECG (Lead I), and apical sound tracing from patient with severe aortic stenosis and no mitral valvular disease. The curves have been replotted from the original data so that they are superimposed on a single pressure-time plot. The maximal pressure gradient across the aortic valve during systole is more than 100 mm. Hg. A small pressure gradient during the early part of ventricular diastole exists across the mitral valve. During the remainder of diastole there is no significant gradient across the mitral valve.

RESULTS AND DISCUSSION

In the earliest studies, pressure measurements alone were made. Mitral stenosis was the only abnormality which could be consistently evaluated with accuracy although the presence of severe aortic stenosis could also be determined. In most patients with mitral stenosis, the pressure curves, taken simultaneously from the atrium and ventricle, show a positive gradient across the mitral valve throughout diastole (Fig. 6). The presence of any positive gradient across the valve at the end of ventricular diastole has, in all instances, been associated with mitral stenosis. Gradients during the earlier part of diastole which do not persist through the end-diastolic period have not been of equal diagnostic significance (Fig. 7). In general, the size of the mean gradient has been fairly well correlated with the degree of stenosis as estimated later at the time of operation. When the stenosis has been severe, the gradient has been relatively constant throughout diastole. Evaluation of the presence and severity of lesser degrees of aortic stenosis from pressure curves alone has been less satisfactory, although pressure gradients across the aortic valve of greater than 100 mm. Hg have been recorded and have

Fig. 6.



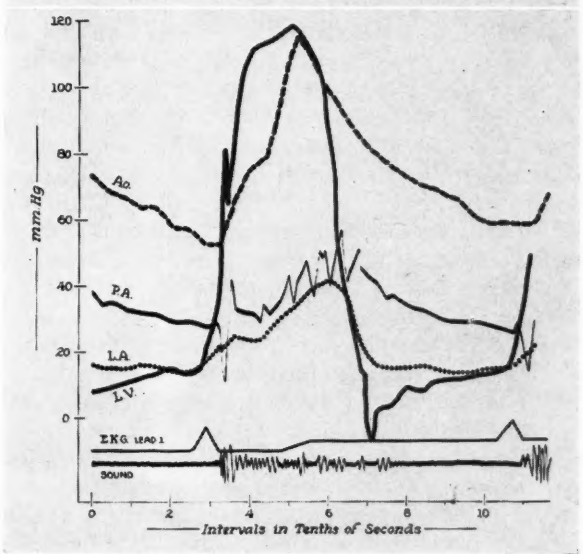


Fig. 7.

Fig. 6.—Left atrial (*LA*), and left ventricular (*LV*) pressure curves and ECG (Lead II) from a patient with severe mitral stenosis. The left atrial pressure is persistently higher than left ventricular pressure through diastole (approximately 10 mm. Hg) but this relation does not hold during the diastole preceding the ventricular premature beat.

Fig. 7.—Replotted pressure curves from the aorta (*Ao*), pulmonary artery (*PA*), left atrium (*LA*), and left ventricle (*LV*), electrocardiogram (Lead I), and phonocardiogram (sound) from a patient with mitral insufficiency by clinical evaluation and an undetermined degree of mitral stenosis and aortic stenosis and insufficiency. The early systolic gradient across the aortic valve and the slightly prolonged gradient across the mitral valve during diastole are difficult to correlate with the presence and severity of the valvular disease.

been consistently indicative of severe aortic stenosis (Fig. 5). Arterial pulse curves have also been analyzed in detail by others[24, 25] in an effort to find an easy way of estimating valve orifice size in patients with aortic stenosis but no simple analysis of pulse pressure curves alone has as yet proved to have clinical value.

At the same time, the early results when correlated with findings at operation made apparent the inadequacy of assessing certain types of valvular abnormalities on the basis of pressure data alone, it was also apparent that stroke volume and cardiac rate were additional variables in the estimation of the size of the valvular orifice. As an example, a change in cardiac rate from 60 to 100 per minute gives a considerable change in gradient with the same cardiac output and valve orifice size in patients with aortic stenosis. Measurements of forward and regurgitant flow and the application of hydraulic formulas permit the estimation of valve orifice areas even in the presence of valvular insufficiency. In fact, all flow-pressure-volume relationships can be estimated. In recent studies when these measurements have been utilized, a satisfactory evaluation has been obtained in patients with aortic and mitral stenosis or mitral insufficiency either singly or in combination. The value of combining the pressure and dilution curve data is shown in the following example of a patient with rheumatic aortic and mitral valvular disease. The pressure curves are shown in Fig. 8. A small end-diastolic gradient across the mitral valve was present and there was a mean pressure gradient throughout diastole of 15 mm. Hg. The mean systolic pressure gradient across the aortic valve was 55 mm. Hg. The dilution curves are shown in Figs. 9 and 10. The calculated cardiac output was subnormal, 3.2 L. per minute. The ratio of mixing to total "left-heart" blood volume was 0.21, characteristic of mitral stenosis with little or no insufficiency.[3] A normal residual volume of 72 ml. was calculated for the left ventricle. The curve obtained by sampling from the left atrium following injection into the ventricle indicated only a small amount of mitral insufficiency (Fig. 10). The conclusion regarding the degree of insufficiency was strengthened by the fact that the terminal slope of the K^{42} dilution curve from the brachial artery was normal (Fig. 9). The aortic valve orifice area (during systole) was calculated to be 0.4 sq. cm. and that of the mitral valve (during diastole) was calculated to be 1.1 sq. cm. Thus, the catheterization data were interpreted as indicating significant mitral and aortic stenosis and the presence of a small amount of mitral insufficiency. The findings at operation confirmed that mitral and aortic stenosis and slight mitral insufficiency were present. No aortic insufficiency was detectable.

The problem of estimating satisfactorily the degree of aortic insufficiency has not been studied up to this time and therefore, evaluation of the degree of aortic stenosis, in the presence of appreciable aortic insufficiency, is also difficult. Attempts have been made by others to estimate the degree of aortic insufficiency by angiographic techniques with injection of radiopaque substances into the root of the aorta.[26] Some regurgitant dye can be observed

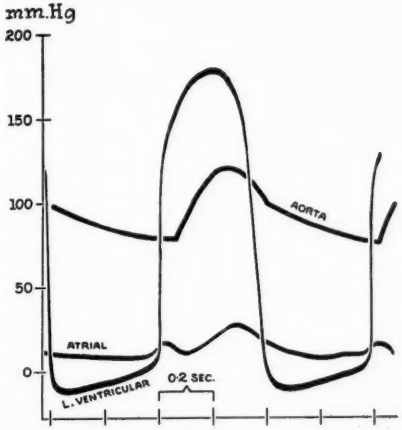


Fig. 8.

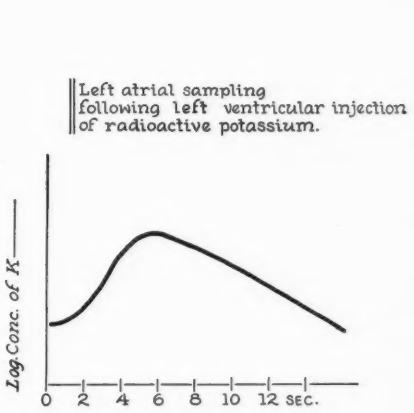


Fig. 9.

Fig. 8.—Left atrial, left ventricular, and aortic pressure curves from patient with aortic and mitral stenosis and slight mitral insufficiency. There is a mean pressure gradient which is about 15 mm. Hg across the mitral valve during diastole and although the gradient persists throughout diastole it is of larger magnitude early in diastole than immediately before ventricular contraction. Note also that the mean pressure gradient across the aortic valve during systole is about 55 mm. Hg.

Fig. 9.—Radio-potassium dilution curves recorded from brachial arterial sampling following injection of K^{42} into left atrial and left ventricular chambers. The relatively steep descent of the terminal slope of both curves is found in patients with mitral stenosis and no appreciable mitral insufficiency. Cardiac output of 3.2 L. per minute and left ventricular residual volume of 72 ml. were calculated from the curves.

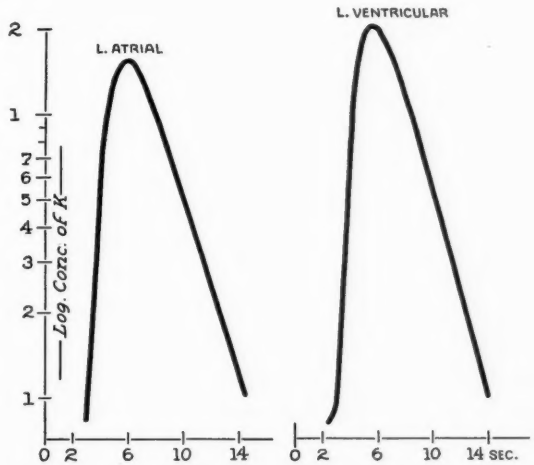


Fig. 10.—Radio-potassium dilution curve recorded from blood sampled from the left atrial blood following injection of K^{42} into left ventricular cavity. The finding of any radioactivity here within the first few seconds following injection of K^{42} into the left ventricular cavity is indicative of mitral insufficiency. The actual concentration values (not shown here) when compared with peripheral arterial values indicated only slight mitral insufficiency.

from the films. We believe that the degree of aortic regurgitation could be quantitatively estimated either in a manner similar to the technique described above for measuring the amount of mitral regurgitation, or by the Korner-Shillingford approach[27] if an indicator-dilution technique is applied. That is, indicator (T-1824, I^{131}, K^{42}) can be injected into the root of the aorta and the relative areas of dilution curves obtained simultaneously from the left ventricle and peripheral artery can be compared, or the variance from normal of the peripherally recorded dilution curve can be analyzed by the method of power formulations.

Another major problem remaining is that of proving the correctness of the assumption that the measured left atrial time-concentration curve for K^{42} activity, following left ventricular injection, is truly related to the amount of blood regurgitating into the left atrium. For example, if the needle tip is only partially in the regurgitant jet or is in atrial blood with which it mixes, the calculated volume of regurgitation will be too small or not even detected. Studies in dogs with small atria apparently show that insufficiency can be satisfactorily estimated,[21] but our experiences with patients having mitral insufficiency and large atria who have undergone surgery are too limited to permit one to reach any over-all conclusions.

As indicated previously, these studies have also provided information about left heart chamber and aortic volumes and about mechanisms responsible for the mitral first sound and for gallop rhythm. In studies reported in detail elsewhere,[3] it was noted that the "left-heart" volumes and circulation times were elevated in all patients with mitral valvular disease. The largest volumes were found in mitral insufficiency where the left atria were largest and where there may be sufficient interchange of blood between the atrium and ventricle so that the "left-heart" functions much as a single chamber. As a consequence, the recorded circulation times from atrium and ventricle to peripheral artery, respectively, were almost identical. In contrast, except for the frequent finding of reduced cardiac output, patients with pure mitral stenosis and atrial fibrillation have shown only an increased left atrium to femoral artery total blood volume and circulation time. These findings are compatible with the concept that in patients with mitral stenosis and atrial fibrillation atrial flow is laminar, as in normal subjects, and that the only important volume derangement is an increase in left atrial volume.

The phonocardiographic tracings in patients with mitral stenosis show that closure of the mitral valve occurs sometime after the onset of ventricular systole during the period when the rate of rise of the ventricular pressure is great (see Fig. 6). This is in contrast to the situation in patients without mitral stenosis in which mitral closure occurs at the onset of ventricular systole when ventricular pressure is increasing at a slower rate (see Fig. 5). These findings may account for the lateness and the loud and snapping character of the first heart sound in mitral stenosis. Studies of patients with mitral insufficiency who exhibit gallop sounds have disclosed a large pressure gradient, and presumably a maximum blood flow between the atrium and ventricle at the time of the extra sound. These observations indicate that

the sound is probably produced by a sudden impact on, or stretching of, the ventricle from the rapid inflow of blood and that it is probably not related to momentary reflux closure of atrioventricular valves as has been proposed by others.[28]

It may be concluded that the physiologic data available from these methods may have as great a value in increasing the understanding of hemodynamics in rheumatic valvular disease as in providing an accurate preoperative diagnosis. From such information, better and simpler diagnostic techniques and tools will be forthcoming. Recently, new equipment has been designed which can be used in the operating room with minimal explosion hazard and which should provide an accurate, simple, and quick way of obtaining data from patients at the time of operation. In this way, not only can comparative data be obtained from patients previously studied preoperatively because of the need for more precise preoperative evaluation, but additional data can also be obtained from these patients in whom a satisfactory preoperative diagnosis has been made without left heart catheterization and the surgeon can be provided with immediate objective evidence concerning the mechanical effectiveness of his operative procedure.

Since, in most patients, a satisfactory preoperative cardiac evaluation can be achieved without resorting to catheterization of the left side of the heart, which may have dangerous complications, the routine use of this method for the sole purpose of gathering data or even for the purpose of corroborating the diagnosis seems unwarranted.

SUMMARY

A method for catheterization of the left side of the heart has been presented. With this method it is possible to obtain simultaneous measurements of pressure in the left atrium, ventricle and aorta and to obtain indicator-dilution curves from various injection and sampling sites in the left side of the heart or the large arteries. From these measurements, aortic and mitral transvalvular pressure gradients and forward and regurgitant blood flow and left atrial, ventricular and aortic volumes can be determined. When used with proper hydraulic formulas, an estimation of valve orifice area can be calculated using these data. It appears that in patients with aortic stenosis, mitral stenosis, and mitral insufficiency proper diagnosis of the anatomic lesions present and their severity can be made consistently. Methods for evaluating aortic insufficiency are under study. The possibility of serious complications from this technique, although slight, and the ability of the experienced physician to achieve in most instances a proper cardiac evaluation by other means should restrict the use of catheterization of the left heart to those cases in which other studies have failed to provide a satisfactory diagnosis.

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(For Discussion, see page 464)

THE EFFECT OF EXERCISE UPON THE MEAN DIASTOLIC LEFT ATRIAL-LEFT VENTRICULAR GRADIENT IN MITRAL STENOSIS

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INTRODUCTION

IT has been demonstrated during the course of combined right and left heart catheterization that the physiologic definition of mitral stenosis is the demonstration of a significant mean diastolic left atrial-left ventricular gradient. In subjects with tight mitral stenosis, left heart catheterization data at rest can provide satisfactory physiologic corroboration of the lesion. Since the magnitude of the diastolic left atrial-left ventricular gradient is determined by three factors, i.e., heart rate and the diastolic flow across the valve, in addition to mitral valve size, it has become necessary in some subjects to explore the meaning of a small gradient at rest by determination of this variable during the stress provided by bicycle exercise.

The purpose of this report is to present data obtained during combined left and right heart catheterization relative to the parameters of gradient, cardiac output, and heart rate, both at rest and during exercise, in patients with mitral stenosis.

METHODS

Right heart catheterization and arterial cannulation are performed via the same arm in the usual manner in the basal postabsorptive state to permit determination of cardiac output by the Fick principle. Multiple steady-state pressure and cardiac output determinations are made at rest and during exercise and recovery. Whenever possible, double-lumen or triple-lumen catheters are used to permit simultaneous pressure recording from multiple sites in the right heart and pulmonary artery. With the right heart catheter and brachial artery needle in situ, the patient is turned to the prone position. Repeat right heart pressures are obtained. Meperidine hydrochloride (50 to 75 mg.) is given intramuscularly at this point.

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Read at the Thirty-seventh Annual Meeting of The American Association for Thoracic Surgery at Chicago, Ill., May 4-7, 1957.

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Left heart catheterization is performed by a modification of the posterior percutaneous puncture technique of Fisher.[1] Fluoroscopic visualization of the left atrium is carried out in the prone position. Two 6 to 8 inch No. 17 thin-walled styletted needles are inserted into the left atrium. Polyethylene tubing is then passed through these needles into the left atrium and left ventricle. Simultaneous pressures are obtained (from the same base line and at identical strain gauge sensitivities[2]) from the left atrium, left ventricle, and brachial artery in the prone position.

Wherever possible, the left heart needles are removed at this point in such a fashion that the polyethylene catheters remain in the left atrium and left ventricle, respectively. The patient is carefully returned to the supine position. These positional changes are facilitated by the prior insertion of the brachial artery needle and right heart catheter in the same arm, thereby leaving the other upper extremity free to aid in the changes in position. After a suitable rest period to permit return to the steady state, repeat measurements of right and left heart pressures and cardiac output and rate are performed at rest and exercise.

All pressure measurements are made on a 6-channel photographic recorder* employing Statham strain gauges P23AA, P23D, and more recently P23G. Blood gas analysis is performed by standard techniques on a Van Slyke manometric apparatus. Expired gas analyses are carried out with a Scholander gas analyzer.

In the supine position, the reference level for right heart pressures is 5 cm. dorsal to the angle of Lewis. In the prone position, the reference level is also 5 cm. dorsal to this angle. A level 10 cm. dorsal to the angle of Lewis has been adopted as the zero level for left heart pressure in this study in both supine and prone positions.

MATERIALS

Fifty-two simultaneous combined right and left heart catheterizations have been performed to date in 44 patients, 31 of whom had mitral valve disease. Fifteen studies in 14 patients have been selected for presentation in this paper. These 14 subjects constitute the group in which pressure and output data at rest and exercise are available during combined heart catheterization.

Eight patients have been investigated prior to possible commissurotomy. Three subjects have been sent to surgery,† 2 are awaiting commissurotomy, and 2 have been rejected for surgery. The eighth patient is asymptomatic and is not being considered for surgery at this time.

Seven patients were studied at varying intervals after mitral surgery; one (L. K.) had combined heart catheterization with rest and exercise

*Electronics for Medicine, White Plains, New York.

†These patients (and others in the over-all series) have been operated upon by various surgeons including Drs. Robert S. Litwak, DeWitt C. Daughtry, Francis N. Cooke, and Myron I. Segal.

data, preoperatively. The physical characteristics of these 14 patients are given in Table I. All subjects were on digitalis therapy at the time of study and none were in clinical heart failure.

TABLE I. PHYSICAL CHARACTERISTICS AND DIAGNOSIS IN FOURTEEN CASES OF MITRAL STENOSIS

CASE NO.	SEX	AGE (YR.)	B.S.A. ($M.^2$)	DIAGNOSIS	COMMENT
53 W. McB.	M	49	1.62	Rh.H.D., As.H.D., E.H., M.S., old anterior wall myocardial infarction, A.F., III D	Complicated by nonobstructive pulmonary emphysema
56 P. M.	F	49	1.52	Rh.H.D., E.H., M.S., M.I., A.I., A.F., III C	L.V.H. on fluoroscopy and ECG
58 S. J.	M	34	1.73	Rh.H.D., E.H., M.S., minimal A.S., A.F., III C	Difficult to control ventricular rate; minimal L.V.-B.A. systolic gradient
63 F. L.	M	21	1.60	Rh.H.D., E.H., M.S., minimal A.I., N.S.R., II C	R.V.H. but not L.V.H on fluoroscopy
73 A. G.	F	30	1.46	Rh.H.D., E.H., M.S., N.S.R., I B	Completely asymptomatic
69 S. B.	F	53	1.41	Rh. H.D., E.H., M.S., minimal A.S., A.F., II C	Arterial emboli; minimal L.V.-B.A. systolic gradient
81 T. R.	M	42	1.85	Rh.H.D., E.H., M.S., N.S.R., Graham Steel murmur, III D	Diastolic apical rumble not heard
51 L. K.	F	33	1.65	Rh.H.D., E.H., M.S., A.F., II C	Previous arterial emboli; also studied 9 weeks after commissurotomy
36 R. R.	F	30	1.55	Rh.H.D., E.H., M.S., N.S.R., I B	1 mo. postcommissurotomy; III C preop.
42 S. W.	M	34	1.93	Rh.H.D., E.H., M.S., minimal M.I., A.F., I B	Minimal M.I. preop.; R.V.H., but not L.V.H. on fluoroscopy, III C preop.; 9 weeks postcommissurotomy
60 E. M.	F	37	1.52	Rh.H.D., E.H., M.S., NSR, I B	1 year postcommissurotomy; II C preop.
70 A. L.	F	59	1.52	Rh.H.D., E.H., M.I., M.S., A.F., III C	2 years postcommissurotomy; postop. M.I.
25 D. D.	M	40	1.73	RhH.D., E.H., M.S., N.S.R., I B	10 mo. postcommissurotomy; III C preop.
21 J. V.	F	32	1.55	Rh.H.D., E.H., M.S., minimal M.I., N.S.R., I B	1 year postcommissurotomy; minimal postop. M.I.

Numbers and letters following cardiac diagnoses refer to functional and therapeutic classification.

B.S.A. = Body surface area.
M.S. = Mitral stenosis.
As.H.D. = Arteriosclerotic heart disease.
Rh.H.D. = Rheumatic heart disease.
M.I. = Mitral insufficiency.
E.H. = Enlarged heart.
A F. = Atrial fibrillation.
A.S. = Aortic stenosis.
A.I. = Aortic insufficiency.
N.S.R. = Normal sinus rhythm.
L.V.H. = Left ventricular hypertrophy.
R.V.H. = Right ventricular hypertrophy.

RESULTS

The data relative to cardiac output and intracardiac pressure levels at rest and during exercise are presented in Tables II and III. The average cardiac index, oxygen consumption, arteriovenous oxygen difference, and respiratory quotient are 2.28 L./min./M.^{2}, 123 ml./min./M.^{2}, 5.5 volumes per cent and 0.83, respectively, for the 8 preoperative studies, and 2.61 L./min./M.^{2}, 120 ml./min./M.^{2}, 4.9 volumes per cent, and 0.82, respectively, for the 7 postoperative studies. These flow values were obtained in the supine position with both right and left heart catheters in situ. The data obtained during right heart catheterization alone earlier in the study are not listed.

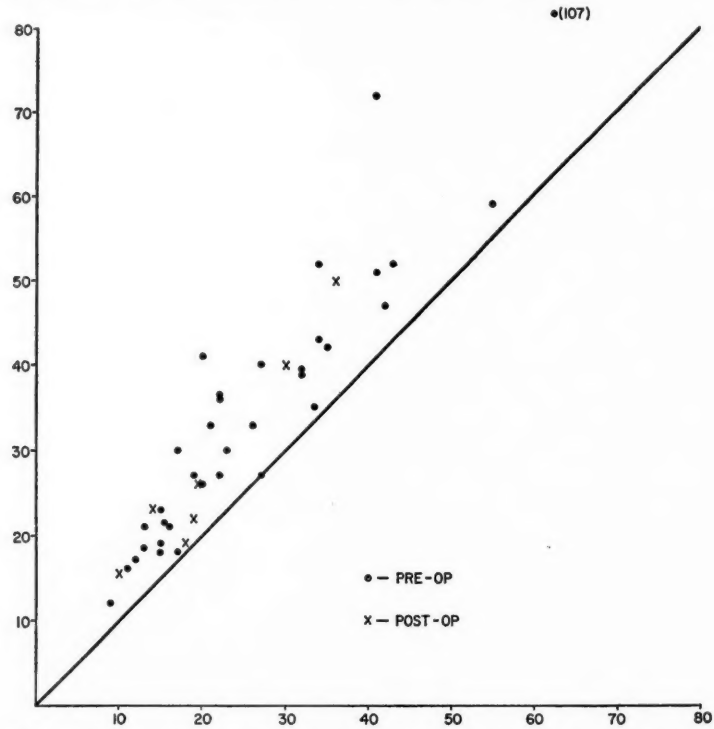

Fig. 1.—Mean pulmonary artery pressure, supine (abscissa), during right heart catheterization plotted against the same variable, prone, before left heart catheterization (ordinate). The difference is significant, P< .01. The average difference is 9 mm. Hg.

The average left atrial-left ventricular mean diastolic gradient in the preoperative studies is 10 mm. Hg (range 6 to 22) at rest and 18 mm. Hg (range 13 to 33) during exercise, excluding the data in the asymptomatic patient (A. G.). The corresponding figures in the postoperative group are 2 mm. Hg (range 1 to 3) at rest and 5 mm. Hg (range 2 to 8) during exercise. The mean left atrial pressure in the preoperative group is 20 mm. Hg (range 15 to 28) at rest and 28 mm. Hg (range 20 to 37) during exercise. The

corresponding data in the 7 postoperative studies is 9 mm. Hg (range 5 to 14) at rest and 11 mm. Hg (range 6 to 20) during exercise. Two of the 8 subjects investigated preoperatively had mean pulmonary artery wedge pressures at the upper limits of normal (11 and 12 mm. Hg) despite gradients of 8 and 15 mm. Hg, and 9 and 23 mm. Hg at rest and exercise, respectively.

The effect of position on mean pulmonary artery pressure is depicted in Figs. 1 and 2. In Fig. 1, the mean pulmonary artery pressure in the prone position before insertion of the left heart needles is plotted on the ordinate and the same pressure in the supine position during right heart catheterization alone is plotted on the abscissa. In Fig. 2, the abscissa is similar while

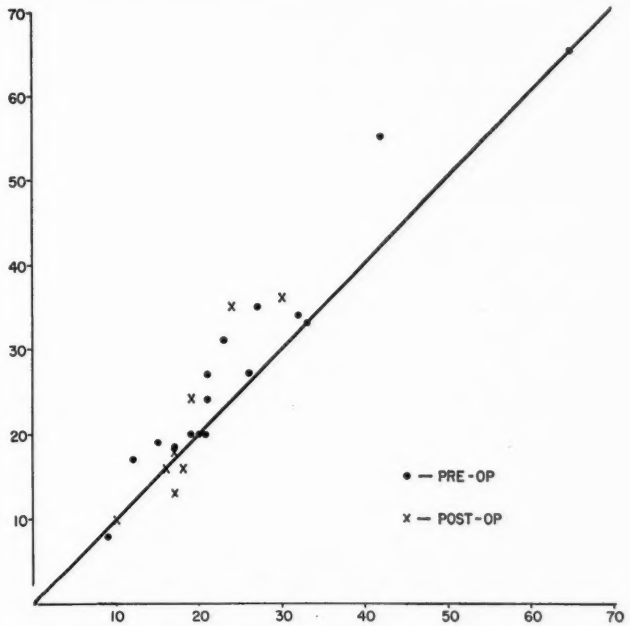

Fig. 2.—The abscissa is similar to that in Fig. 1. The ordinate is mean pulmonary artery pressure, supine, after combined heart catheterization. The difference is significant. P< .01, but the average difference is only 3 mm. Hg.

the ordinate is the mean pulmonary artery pressure in the supine position during combined right and left heart catheterization. Pulmonary artery mean pressure in the prone position is significantly greater than that during the right heart study alone ($P < .01$). The average rise is 9.2 mm. Hg. Pulmonary artery mean pressure in the supine position during combined heart catheterization is also significantly greater than during right heart catheterization alone ($P < .01$), but the average rise is only 3 mm. Hg. Comparison of the mean pulmonary artery pressure (prone) with that supine during combined heart catheterization reveals a mean fall of 4.5 mm. Hg ($.01 < P < .05$).

TABLE II. CARDIAC OUTPUT DATA IN FOURTEEN CASES OF MITRAL STENOSIS DURING COMBINED HEART CATHETERIZATION

CASE NO.		HEART RATE (BEATS/MIN.)	CARDIAC INDEX (L./MIN./M.^{2})	STROKE VOLUME (ML./BEAT)	O_2 CONSUMPTION (ML./MIN./M.^{2})	R	A-V DIFFERENCE (VOL. %)	ARTERIAL SAT. (%)
53	R	63	1.78	46	115	.85	6.5	93
	E	120	1.95	26	224	.99	11.5	93
56	R	65	1.94	45	111	.72	5.7	96
	E	90	2.77	47	226	.75	8.2	96
58	R	143	2.37	29	138	.81	5.8	94
	E	152	2.70	31	227	.84	8.4	95
63	R	60	2.99	80	123	.90	4.1	94
	E	72	3.06	68	208	.90	6.8	97
73	R	76	2.47	48	114	.89	4.6	96
	E	88	2.63	44	200	.90	7.6	95
69	R	75	2.16	41	112	.82	5.2	95
	E	--	---	--	---	--	---	--
81	R	97	1.99	38	154	.81	7.7	86
	E	108	2.14	37	221	.88	10.3	88
51*	R	101	2.56	42	119	.80	4.6	97
	E	101	3.26	53	196	.79	6.0	94
51†	R	103	2.24	36	112	.89	5.0	95
	E	114	2.77	40	227	.85	8.2	94
36	R	77	3.87	66	120	.88	3.1	98
	E	105	4.47	66	259	.96	5.8	98
42	R	71	2.73	75	137	.83	5.1	92
	E	135	3.70	53	359	1.03	9.7	93
60	R	76	3.47	69	125	.78	3.6	97
	E	100	4.78	73	268	.90	5.6	97
70	R	68	1.24	28	87	.85	7.0	93
	E	84	1.87	34	193	.90	10.3	93
25	R	70	2.48	62	128	.72	5.2	96
	E	88	3.33	65	320	.82	9.6	96
21	R	75	2.28	47	128	.76	5.6	98
	E	84	3.10	57	245	.87	7.9	97

*Preoperative. †Nine weeks postoperative.

TABLE III. HEMODYNAMIC DATA IN FOURTEEN CASES OF MITRAL STENOSIS DURING COMBINED HEART CATHETERIZATION

CASE NO.		HEART RATE (BEATS/ MIN.)	PUL. WEDGE M (MM.Hg)	PUL. ART. S/D, M (MM.Hg)	RT. VENT. S/D (MM.Hg)	RT. ATRIUM M (MM.Hg)	BRACH. ART. S/D, M (MM.Hg)	LEFT VENT. S/D (MM.Hg)	LEFT ATRIUM M (MM.Hg)	LA-LV DIASTOLIC MEAN GRADIENT (MM. Hg)
53	R	52	12	56/25, 36	56/3	1	104/59, 77	102/9	19	8
	E	115	--	122/51, 68	--	–	109/68, 86	120/11	27	15
56	R	60	11	38/14, 20	38/3	1	130/59, 83	114/6	16	9
	E	86	--	65/33, 43	65/1	–	--	122/2	27	23
58	R	120	20	43/28, 33	43/6	–	102/79, 88	107/8	27	14
	E	160	--	72/47, 54	70/6	–	--	113/8	37	21
63	R	57	15	41/19, 24	40/6	2‡	122/58, 86	105/16§	19	7
	E	78	--	65/28, --	64/7	3‡	127/70, 93	117/14	28	13
73	R	72	12	29/12, 18	29/7	–	105/60, 77	98/11	16	4
	E	90	--	39/17, 24	40/7	–	--	99/12	20	6
69	R	67	15	32/14, 20	32/3	3	115/65, 83	118/12	18	6
	E	150	--	59/30, 36	--	–	132/81, 98	138/12	30	16
81	R	87	28	96/42, 61	96/6	4	110/67, 84	93/6	28	22
	E	104	--	136/60, 87	--	–	--	98/3	33	33
51*	R	98	14	35/16, 21	35/2	3	110/62, 79	97/6	15	8
	E	98	--	47/23, 32	47/3	–	119/74, 91	103/8	22	13
51†	R	102	7	25/14, 18	25/4	5	120/84, 101	112/10	12	3
	E	102	--	36/22, 28	36/6	–	135/91, 105	129/11	16	5
36	R	75	--	31/13, 21	31/5	2	118/66, 86	116/11	10	3
	E	89	--	39/20, 26	39/3	–	136/70, 95	121/9	10	6
42	R	73	--	45/27, 35	45/3	–	130/77, 94	129/11	14	2
	E	138	--	71/44, 56	70/4	–	136/77, 94	125/9	20	7
60	R	70	3	33/13, 18	33/4	0‡	138/80, 103	128/12	9	3
	E	95	--	48/20, 28	48/4	0‡	151/75, 104	134/9	12	8
70	R	63	4	29/12, 17	30/1	3	156/78, 101	154/3	5	2
	E	96	--	47/19, 27	--	–	172/84, 114	169/4	6	4
25	R	68	15	44/12, 25	44/5	–	129/72, 93	126/8	8	1
	E	87	--	62/21, 36	62/5	–	138/71, 95	125/9	8	3
21	R	74	3	16/6, 9	17/–1	–2	124/69, 89	105/7	6	1
	E	88	--	25/9, 13	--	–	136/70, 96	125/8	8	2

*Preoperative. †Nine weeks postoperative. ‡Z point of R.A. = end-diastolic R.V. §Minimal A.I. present.

The relationship between flow and atrioventricular pressure gradients is shown in Fig. 3. There is a clear separation between the pre- and postoperative cases except for A. G., the asymptomatic unoperated subject. The slope of the gradient rise per unit increase in flow is considerably greater in the presurgical studies.

Because of the persistent discussion relative to the interpretation of pulmonary artery wedge pressures, these pressures are plotted against mean left atrial pressures (supine) in Fig. 4. These pressures were not obtained simultaneously. The 45-degree line of identity represents the ideal relationship if the two pressures were identical. The wide scatter from the line of identity is apparent.

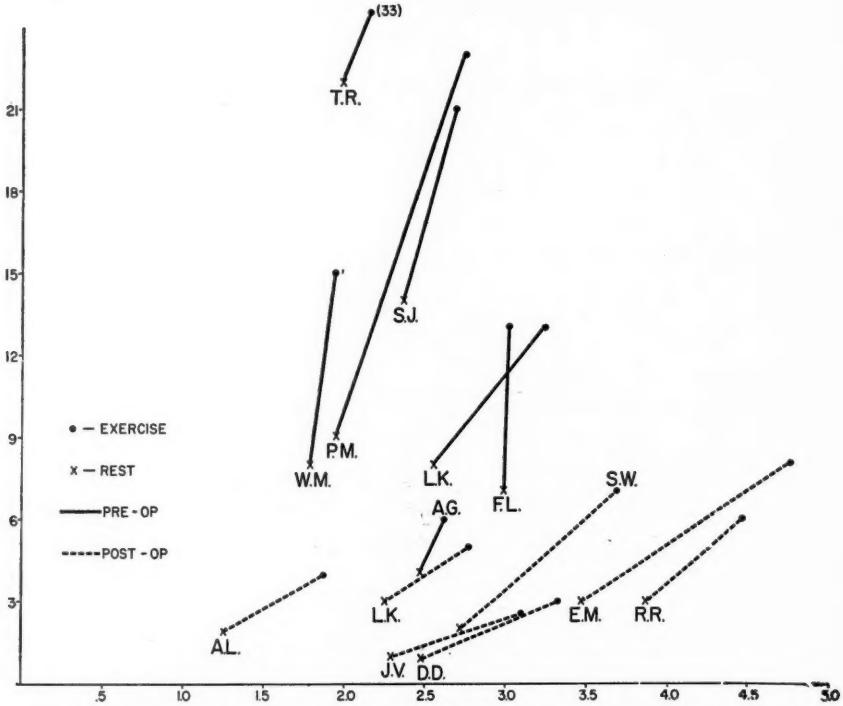

Fig. 3.—Relationship between cardiac index (abscissa) and atrioventricular gradient (ordinate) at rest and exercise. The unbroken lines refer to the preoperative cases; the dotted lines refer to the postoperative studies. × are the points at rest. • are the points during exercise.

The magnitude of the diastolic left atrial-left ventricular gradient is influenced by the position of the patient. This is demonstrated in Fig. 5. The results fall into three groups. In the postoperative studies where the gradients are all at relatively low levels, there is little positional change. However, a striking change in the level of the gradient is noted in about half of the subjects studied preoperatively.

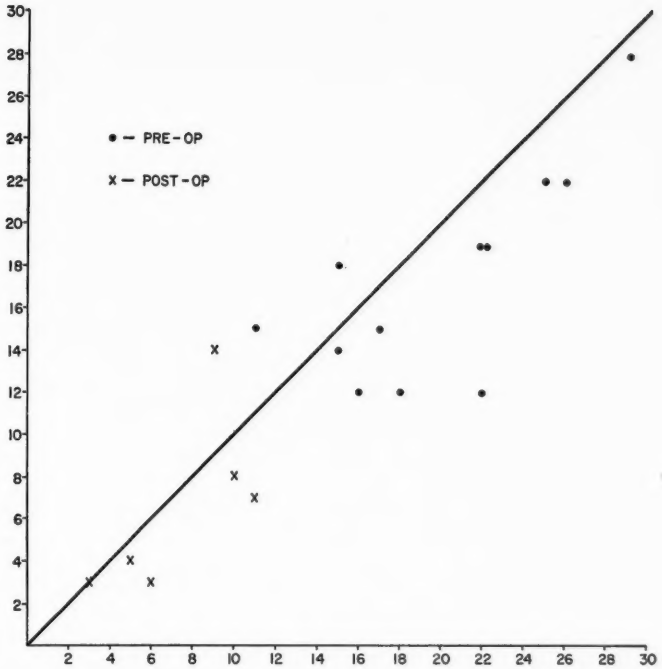

Fig. 4.—The wide divergence from the 45 degree line of identity between mean left atrial pressure, supine (abscissa), and mean pulmonary artery wedge pressure (ordinate), supine, is readily seen.

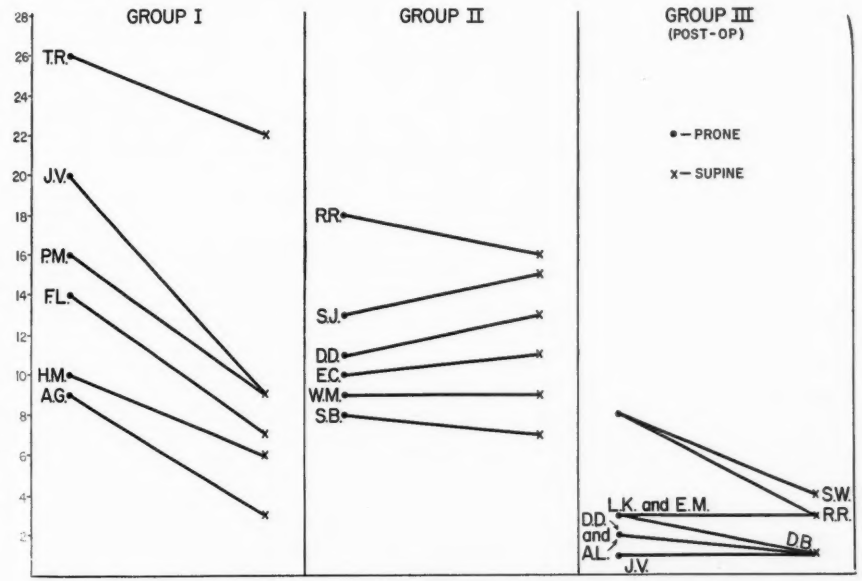

Fig. 5.—The effect of position upon the mean diastolic left atrial-left ventricular gradient. The results fall into three groups (see text).

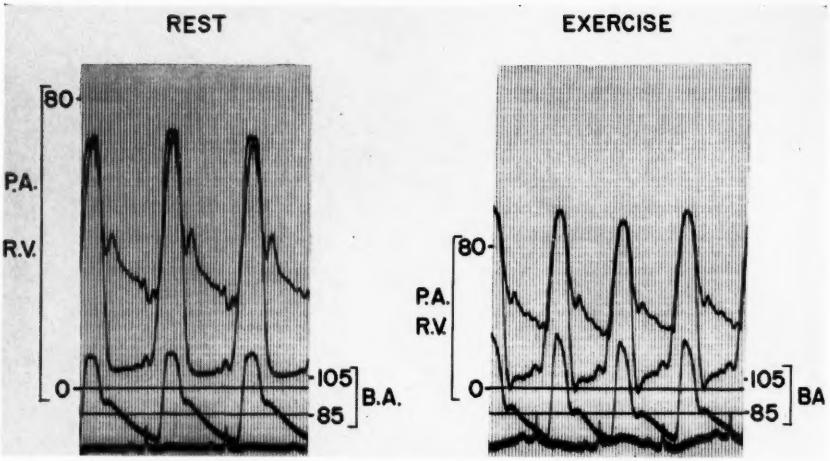

Fig. 6.—Preoperative heart catheterization data in D. D. The marked pulmonary hypertension at rest, with a further increase during exercise, is readily seen.

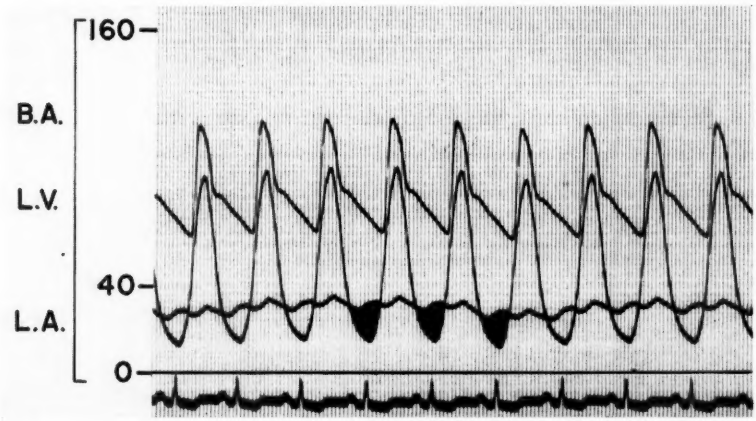

Fig. 7.—Left heart pressure curves, preoperatively, in D. D. The shaded areas represent the diastolic left atrial-left ventricular gradient.

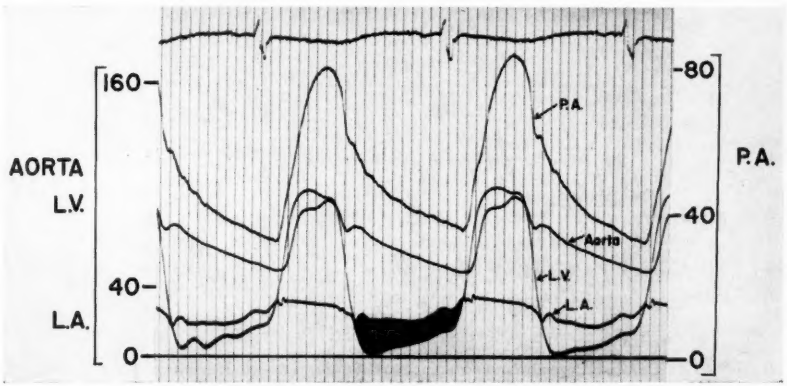

Fig. 8.—Operating room, precommissurotomy, right and left heart pressures in D. D.

The data illustrated in Figs. 1, 2, 4, and 5 are taken from the over-all series of combined heart catheterizations and therefore include patients other than the 14 who comprised the major body of subject material of this report.

The clinical value of combined heart catheterization is illustrated in Figs. 6-14. The paper speed in these figures is either 25 or 75 mm. per second. The

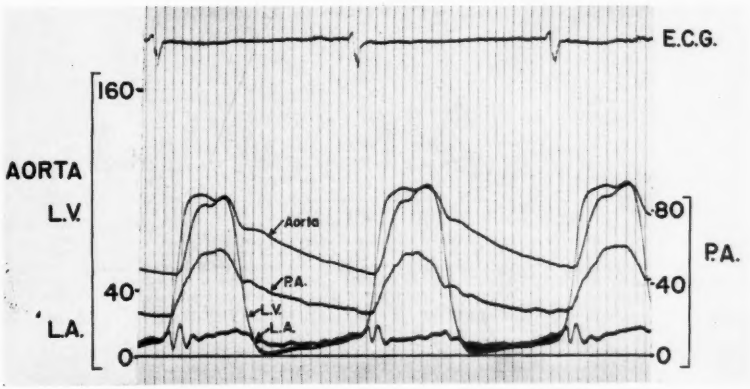

Fig. 9.—Operating room, postcommissurotomy, right and left heart pressures. Marked diminution in the magnitude of the gradient is noted.

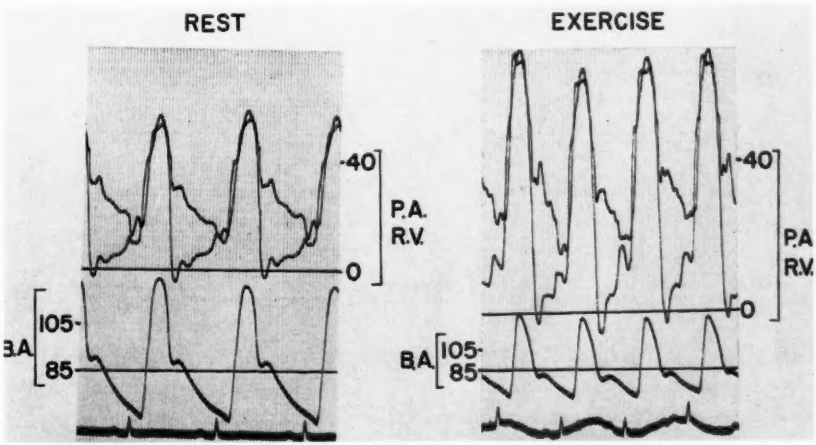

Fig. 10.—Right heart catheterization data one month postoperatively. Pulmonary hypertension persists at rest with a further rise during exercise, although at a lower level than preoperatively.

preoperative right heart pressures at rest and exercise are shown in Fig. 6 in D. D. There is marked pulmonary hypertension at rest with a further increase during exercise. The left atrial-left ventricular diastolic gradient is depicted in Fig. 7. The left ventricular curve is somewhat damped. The

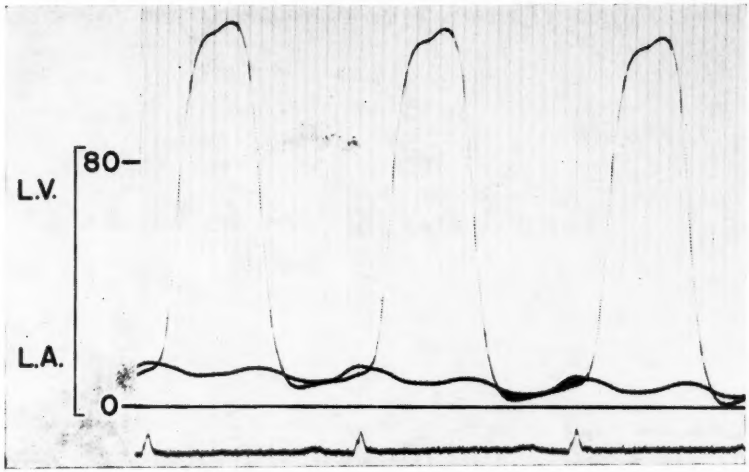

Fig. 11.—Left heart curves, prone, in D. D., one month postoperatively. A small gradient (2 mm. Hg) persists.

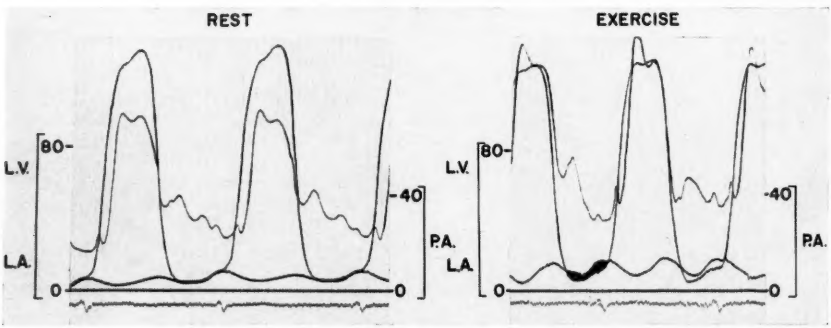

Fig. 12.—Left heart curves at rest and exercise, supine, in D. D. one month after surgery. Note the decrease in the left atrial-left ventricular gradient at rest, supine, compared to the value at rest, prone. There is a slight increase (to 4 mm. Hg) during exercise.

operating room precommissurotomy pressures are shown in Fig. 8 and the postcommissurotomy curves in Fig. 9. The marked gradient decrease is readily seen. On repeat catheterization one month after surgery, there is persistent pulmonary hypertension at rest and exercise (Fig. 10) despite the fact that the gradient has been almost completely abolished. At this time, the gradient is 2 mm. Hg prone at rest (Fig. 11), less than 1 mm. Hg at rest supine, but increases to 4 mm. Hg during exercise (Fig. 12). These gradient data persisted unchanged 10 months after surgery. The combined heart data in L. K. (preoperative) are shown in Fig. 13. The atrioventricular gradient is 8 mm. Hg at rest but rises to 13 mm. Hg during exercise (Fig. 14).

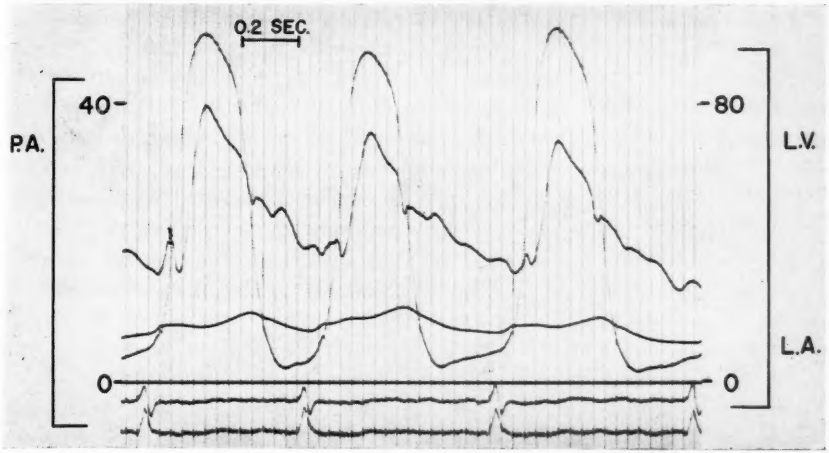

Fig. 13.—Preoperative right and left heart pressure curves in L. K. (supine). The resting atrioventricular gradient is 8 mm. Hg.

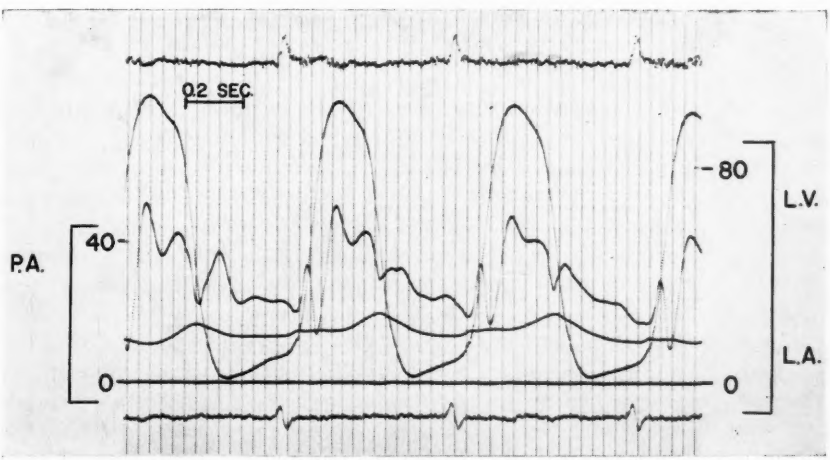

Fig. 14.—The atrioventricular gradient during exercise has risen to 13 mm. Hg (L. K., preoperative).

DISCUSSION

In the past, right heart catheterization provided a valuable though necessarily limited view of the abnormal hemodynamic state existing in patients with mitral stenosis.[3, 4] The development of left heart catheterization[1, 5-7] afforded a more direct approach to the disturbed physiology. Combined simultaneous right and left heart catheterization has been the next logical developmental step for it permits more precise physiologic interpretation of the meaning of the left atrial-left ventricular gradient in terms of cardiac rate and flow across the valve.

The resting cardiac outputs, determined during combined heart catheterization in the 14 patients in this report, agreed closely with those obtained during right heart catheterization alone earlier in the study, in all but one instance, demonstrating that the steady state, as defined by Fishman and his associates,[8] may be achieved during combined right and left heart catheterization. These data will be presented in detail in a future report.

Pulmonary artery wedge pressure has been considered "to be a moderately damped but reasonably accurate representation of the left atrial pulse, in pressure and usually in contour."[9, 10] Frequent exceptions to this concept have been observed during the course of this study. Two instances of normal pulmonary artery wedge pressure at rest in the presence of significant left atrial hypertension and left atrial-left ventricular mean diastolic gradients at rest and exercise have been noted (see Table III). Similar observations have been made in 3 other subjects in this laboratory. Furthermore, a mean pulmonary artery wedge pressure of 14 mm. Hg has been observed in one postoperative study in which the gradient was 1 mm. Hg at rest and 3 during exercise in the presence of a normal left ventricular end-diastolic pressure. The criteria employed for deciding that the catheter tip was in the pulmonary artery wedge position are in general similar to those of Connolly and Wood.[10]

The effect of patient position, i.e., prone or supine, on intracardiac pressure levels is of importance in view of the variations in technique of performing combined heart catheterization in different laboratories.[11-13] The results of this study demonstrate a distinct rise (9 mm. Hg) in mean pulmonary artery pressure when the patient is turned from the supine to the prone position even before the left heart needles are inserted. The magnitude of this change is too large to be ascribed to differences in the level of zero pressure in the two positions. Furthermore, on return to the supine position there is an average fall of 4.5 mm. Hg in the mean pulmonary artery pressure. That the procedure of left heart catheterization per se does not result in appreciable elevation in mean pulmonary artery pressure is demonstrated by the fact that mean pulmonary artery pressure (supine) during right heart catheterization alone is only 3 mm. Hg less than the corresponding pressure during combined heart catheterization (supine). In addition, the left atrial-left ventricular mean diastolic gradient in the supine position is significantly less ($P < .01$) than the gradient in the prone position. These data suggest that the supine position affords a more basal position in which left heart catheterization may be conducted than does the prone position. Because of the pressure variations in the two positions, definitive measurements are performed in the supine position whenever possible. It should be emphasized, however, that it is not always possible to repeat left and right heart pressure measurements, after return to the supine position, for various reasons. These include patient discomfort, length of the over-all catheterization procedure, and inadvertent slipping back of the left ventricular catheter into the left atrium during the period of turning the patient from the prone to the supine position.

The role of pulmonary vascular disease in the production and maintenance of pulmonary hypertension in patients with mitral stenosis is well illustrated by the studies in D. D. The preoperative pulmonary artery systolic pressure was 75 mm. Hg at rest, with a rise to 103 mm. Hg during exercise (see Fig. 6). After surgery, the left atrial-left ventricular mean diastolic gradient was almost completely abolished (see Figs. 9 and 12). However, in the first postoperative study (one month after surgery) the systolic pulmonary artery pressure was 52 mm. Hg at rest and 70 mm. Hg on exercise (see Fig. 10). The left ventricular end-diastolic pressure was normal. A third study, 10 months after surgery, revealed a further drop in systolic pulmonary artery pressure (45 mm. Hg at rest and 60 mm. Hg during exercise) while the atrioventricular diastolic gradient remained identical to the first postoperative study. The persistent pulmonary hypertension must therefore be ascribed to pulmonary vascular disease in this patient.

One final point is worthy of emphasis. The exact level at which the left atrial-left ventricular mean diastolic gradients become of clinical and physiologic significance is as yet unknown. The evaluation of a small gradient at rest is difficult. Resolution of this problem is materially aided by widening of the gradient during exercise. Under the latter conditions, mitral commissurotomy can be recommended with more confidence. Evaluation of the completeness of mitral commissurotomy is also more feasible when rest and and exercise measurements of the mean diastolic left atrial-left ventricular gradient cardiac output and heart rate are performed after surgery.

SUMMARY

Combined right and left heart catheterization at rest and exercise has been performed 15 times in 14 patients with mitral stenosis. Measurements of cardiac output, heart rate, and mean diastolic left atrial-left ventricular gradients have been carried out. The clinical and physiologic significance of these data is discussed.

We are indebted to Stanley Dzwonkowski, B.A., and Miss Hazel Stowe, P.N., for technical and nursing aid, and to Miss Iris Kiem, M.S., M.P.H., for analysis of the statistical data.

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Discussion

(Papers by Blakemore [page 436], and Litwak [page 449] and Their Associates)

DR. HARRISON BLACK, Boston, Mass.—I enjoyed both these papers very much and want to make just a few comments about the experience we have had with left heart catheterization at the Peter Bent Brigham Hospital in conjunction with Dr. Lewis Dexter and associates. We have tried various techniques but have had most consistent success with the Fisher technique, introducing the needle through the back in the prone position under fluoroscopic control.

Between November, 1955, and May, 1957, we have carried out left heart catheterization in 137 patients. Both left atrial and left ventricular measurements were obtained in 118 of these. In 5 only the atrium was entered, in 4 only the left ventricle, and in 10 others neither chamber was penetrated. The safety of the procedure is evidenced by the complete absence of cardiac tamponade, cardiac arrest, or death. Blood-tinged pericardial fluid has been a relatively consistent finding at the time of subsequent cardiac exploration but it has been of no clinical significance. In 5, bradycardia and syncope have occurred, presumably due to vagal effect; this has necessitated discontinuation of the procedure in some. Safety would appear to depend on keeping the procedure as simple as possible. We have obtained valuable and definitive information, employing a single needle and catheter in the left atrium without exercising the patient, and have measured the brachial artery rather than central aortic pressure.

There can be no question that this technique has vastly improved our ability to unravel complicated multivalvular problems. In particular, the differential diagnosis of mitral stenosis and insufficiency has been much improved by the use of pressure measurements across the valve combined with dye dilution curves obtained by injection into the left atrium and sampling at the radial artery. The accompanying slide illustrates how the relative degree of stenosis and insufficiency can be quantitated by the use of the Korner-Shillingford regression formula on the data obtained. Many of these observations have been checked by direct assessment of valve function at the operating table and the correlation between the two has been high. As can be seen, the preoperative clinical impression has had the expected incidence of inaccuracy but the catheter study has revealed the true situation.

Several points warrant emphasis. A high value for mean left auricular pressure (up to 30 mm. Hg) and a gradient across the mitral valve (up to 15 mm. Hg) may be found even though mitral insufficiency is the predominating lesion. The values for left

ventricular end-diastolic pressure in such a situation are within normal limits, indicating that the left atrial pressure elevation is not on the basis of left ventricular failure as was formerly believed.

In aortic valvular disease, the mean systolic gradient from left ventricle to brachial artery combined with dye output measurement gives an accurate appraisal of the degree of stenosis and serves to differentiate the patient whose symptoms and cardiac failure are on an arteriosclerotic rather than a valvular basis. It is important to recognize that pressure measurements made on the operating table without benefit of data on flow across the valve are a poor substitute for an accurate study made in the conscious patient whose myocardium is not depressed by anesthesia and the many other variables introduced by the operative exposure. The chart shown indicates that a wide variation in gradient may be found in aortic valves that have the same effective orifice, the difference being accounted for by variations in flow across the valve.

It must be admitted that the technique employed thus far does not serve to differentiate between insufficiency of the aortic and mitral valves, since it measures only the total regurgitation between the point of injection (left atrium) and the point of sampling (brachial artery). It is hoped that left ventricular injection combined with left auricular sampling, as mentioned today, will further sharpen the diagnostic accuracy.

DR. ANDREW G. MORROW, Bethesda, Md.—I would like to congratulate Dr. Blakemore and Dr. Litwak upon their papers; Dr. Blakemore principally for emphasizing the need for determination of cardiac output in conjunction with left heart catheterization and Dr. Litvak for emphasizing the necessity for making these measurements when the patient is in a known physiologic state. As most of you probably know, at the National Heart Institute, left heart catheterization is performed by the transbronchial route. The safety of this method has something to recommend it. As of this moment we have performed something over 500 catheterizations without a significant complication. Mr. Allison and Dr. Facquet have done a great number and the combined series from three clinics now is over 1,200 without a complication. One of the objections to the transbronchial route has been that, when observations were made with the bronchoscope in the trachea, patients could not be considered in a steady basal stage. Accordingly, we have modified our technique. The catheter is passed with the bronchoscope in place and measurements of valve gradient and cardiac output are made. The needle is then removed and the catheter is left in the left ventricle. In about 30 minutes, most patients have returned to a steady basal state. This is confirmed by measurement of the rate of oxygen consumption, after which the gradients and cardiac output can again be measured. Exercise tests and other physiologic studies can of course be done also. Perhaps all this can be summarized in one lantern slide—here is a picture of a happy man with aortic stenosis undergoing transbronchial left heart catheterization.

DR. J. A. BOUGAS, Boston, Mass.—Most procedures are accepted and established in the medical armamentarium when their value outweighs their morbidity and mortality risks. I think we have seen today the values inherent in combined left and right heart catheterization; they are evident in the excellent descriptions of data which can be obtained through use of this physiologic study method. Also attesting to the value of the procedure is the enthusiastic and rapid increase in use of left heart catheterization throughout this country and around the world. It remains, then, to determine what are the morbidities and mortalities.

In a group of 1,770 left heart catheterizations, collected from this country and abroad, there has been a 0.5 per cent mortality. Three out of 9 deaths occurred during surgical attempts to remedy a hypotensive episode presumably caused by cardiac tamponade; in 2 cases, mortality occurred during catheterization, 1 because of air embolus and the other because of rapid tamponade which resulted from an aortic puncture.

Our experience at the New England Deaconess Hospital in Boston has been with 220 cases of left heart catheterization, of which 80 were combined catheterizations similar

to those described by Dr. Litwak. One patient died on the day following catheterization. She was an elderly woman with mitral insufficiency. Complete post-mortem examination failed to reveal any organic cause relating the catheterization to the death, but the patient did have severe atherosclerosis and multiple, old healed myocardial infarctions. We have counted this as the only death in 220 catheterizations of the left heart.

Dr. Litwak has presented a fine study of pressure gradient variations with relation to position. We too have studied this problem, but we have tilted our patients head down or head up. Our investigation was planned to separate the effect of venous return from the multiple factors involved in simple exercise. We have found increased gradients and elevated pulmonary artery pressures when the patient was in the Trendelenburg position. I should like to ask Dr. Litwak if the degree of head-down tilt was controlled when his patients were turned from prone to supine position.

I should like Dr. Blakemore's opinion concerning the influence of left heart needle size upon morbidity.

It is my feeling that, with increased use of combined heart catheterization, technique and instrumentation will be improved; indication for the procedure will be more clearly determined, and the method will take its proper place in contributing to accurate patient diagnosis.

DR. PAUL A. KIRSCHNER, New York, N. Y.—We have been employing the transbronchial method of left heart catheterization using Dr. Morrow's technique. We are indebted to him for many helpful suggestions.

A plastic catheter is inserted into the brachial artery by percutaneous puncture, passed retrograde to the region of the ascending aorta as close as possible to the aortic valve, and its position is localized radiographically by filling it with radiopaque material (Urokon). This records central aortic pressure.

The left atrium is entered transbronchially using Dr. Morrow's needle, and a plastic catheter is passed through the needle into the left atrium, and through the mitral valve into the left ventricle. This catheter records left ventricular pressure.

The needle is then withdrawn over the left ventricular catheter, holding it in place with a long stylet, and a second left atrial puncture is made alongside the catheter. The needle thus records left atrial pressure.

(slide) This shows simultaneous pressures taken from the left side of the heart in a patient with mitral stenosis using strain gauge manometers of equal sensitivities with identical base lines. An 8-channel electronic recorder is used, and includes the electrocardiogram and phonocardiogram. The gradient in diastole between the left ventricle and left atrium is here shown.

(slide) Using an additional channel, we recorded directly the differential pressure in diastole.

(slide) Using a paper speed of 150 mm. per second (instead of 50 mm. per second) the curves are stretched out.

(slide) In this patient with aortic stenosis, the phonocardiogram shows the characteristic diamond-shaped murmur of aortic stenosis. The systolic gradient of 76 mm. Hg between the left ventricle and the aorta across the aortic valve is well demonstrated, and you will note the absence of any gradient across the mitral valve.

One should note that there is a slight delay in the upstroke of the aortic tracing, indicating that the catheter is not as centrally located in the aorta as we would like.

(slide) Finally, with variations in the systolic pressure in the left ventricle, the aortic systolic murmur also shows variations in its contours.

This work has been done by the cardiac catheterization team of the Mount Sinai Hospital in New York.

DR. J. C. DAVILA, Philadelphia, Pa.—I would like to congratulate the essayists on these two interesting papers. Our work has been particularly concerned with the problems of mitral insufficiency. Because of our interest in this subject we have investigated various methods for measuring regurgitant flow.

We have been able to obtain some rather interesting figures on direct measurement of regurgitant flow on the pulse duplicator. It appears that this is often two to four times greater than forward flow.

(slide) We have some dye dilution curves on patients with severe mitral insufficiency, and have found some interesting information insofar as the applicability of this method for measurement of regurgitant flow is concerned. The first curve is a curve following aortic injection of dye; the second, the atrial injection of dye, and the third, the ventricular injection of dye. As you will note, there are significant differences among all three. One can calculate cardiac output and central volumes, but unfortunately residual volume of the ventricle and the atrium are such that the fractionation to separate residual volume, regurgitant volume, and residual volume of the ventricle from that of the atrium is a major problem. Atrial sampling with photoelectric measurement of dye concentration is unsatisfactory because of the factor of uneven mixing. We feel that perhaps detection of the material within the heart using isotope may provide a better method and we are in the process of investigating instruments for this purpose. This approach was suggested by one of our fellows, Dr. Robert Kyle, and we hope it will help in this matter.

We have preferred the transbronchial route for left heart catheterization. The passage of the catheter across the valve seems to be a rather frequent difficulty in mitral insufficiency and I would like to ask Dr. Blakemore what his experience with the percutaneous technique has been.

DR. CHARLES P. BAILEY, Philadelphia, Pa.—I want to congratulate the essayists on their fine presentations of this advanced way of measuring mitral valve function, and to suggest that this might be done more often. We would find frequently with this exercise test, as Dr. Litwak showed so clearly, that residual stenosis is present in most cases after seemingly effective valvular surgery. Furthermore, re-stenosis, as has been pointed out in a very recent article, is a fairly common cause of recurrent symptoms of cardiac insufficiency after mitral valve surgery. I think I estimated the incidence at 20 per cent or more; really, I think it will prove to be around 50 per cent when the figures are finally in. It may take several years. But by the usual technique of valve surgery, whether called commissurotomy, valvuloplasty, valvulotomy, or valvotomy, we cannot relieve stenosis completely.

In over 700 cases of left heart catheterization at our laboratory, death occurred in 5 shortly after the procedure. Two of them did not seem to be due to the technique, occurring at least one day after the study, in individuals who were very ill.

DR. W. S. BLAKEMORE, Philadelphia, Pa. (Closing).—I want to thank the discussors for their remarks and the stimulation they provide. Most of the specific questions are concerned with morbidity and mortality. Unfortunately, no one in this group of discussors represents either of two other methods of catheterizing the left heart—the transventricular route or the suprasternal route, which Radnor still uses. All methods have risks. Dr. Morrow and I have discussed this a number of times, and I have recently learned of a mortality by the transbronchial route occurring in one of the hospitals in Philadelphia. Therefore, since all have some risk, the study by any route should be used only where indicated for the particular patient to be evaluated. The morbidity would probably not be reduced by using two needles. We use a needle about the size of a No. 18 thin-wall. It is smaller than that used by a number of groups who have here reported few complications. We can use fine catheters and get two catheters through this needle.

Although the posterior aspect of the left atrium where the pulmonary veins enter does not move very much during ventricular systole with two needles, it is conceivable that, with contraction, the atrial wall might pull against the transfixing needles and tear.

Concerning the difficulty of passing the catheters across the mitral valve, the catheters we use are handmade and we try to get them soft, yet not so soft that they will damp the transmitted pulse curve. If the catheters are too stiff we have difficulty in getting them through the mitral valve. A flexible catheter may be passed through the valve somewhat more easily. On the other hand, the disadvantage of the flexible catheter which has not been brought out in this discussion is that it will occasionally tie itself in a knot, and if one gets two catheters in the heart and they tie themselves into a knot, an operative procedure is necessary to get them out. This seems to me to be increasing the risk of a diagnostic study. Therefore, we are continuing to use a less flexible catheter. I think that with the continued use of improved techniques for left heart catheterization more and more information will be obtained in a simple fashion.

DR. ROBERT S. LITWAK, Miami, Fla. (Closing).—I should like to thank the discussors for their very kind comments.

Concerning Dr. Bougas' comment, we have taken great pains to avoid tilting the patient inadvertently and I believe that we can ascribe the pressure changes to things other than tilting of the patient. Concerning Dr. Davila's comment about the technical problems encountered in the study of mitral insufficiency, I would like to suggest a technique which avoids the problem of having the ventricular catheter blown out of the left ventricle back into the left atrium. A catheter is passed into the left atrium through a No. 17 thin-wall needle in the usual manner with the patient in the prone position. The needle is then withdrawn so that the catheter remains in situ. The patient is then turned to the supine position and a direct percutaneous left ventricular puncture is carried out and a catheter fed through the needle. The needle can be safely removed and the catheter permitted to remain in the ventricle. Exercise studies can then be accomplished.

SURGICAL CORRECTION OF TRANSPOSITION OF THE AORTA AND THE PULMONARY ARTERY

THOMAS G. BAFFES, M.D. (BY INVITATION), WILLIAM L. RIKER, M.D. (BY INVITATION), ARTHUR DE BOER, M.D. (BY INVITATION), AND WILLIS J. POTTS, M.D.
CHICAGO, ILL.

EVOLUTION of the surgical correction of transposition of the aorta and the pulmonary artery has been difficult and tedious. Hardly a major cardiovascular group exists in this country which has not had one or more of its members devote a great deal of time and energy in that direction, and a number of significant contributions have been made.[1-5] Recently, we have developed an operative procedure which can be applied clinically to this condition with fair success.[6] A report of our clinical experience with 38 cases of transposition of the great vessels comprises the body of this paper. Of even greater significance, however, are the pathologic and physiologic observations which have been brought into sharper focus by this research.

OPERATIVE PROCEDURE

Our patients were treated by transplantation of the right pulmonary veins and the inferior vena cava, shifting them from one atrium to the other. A homologous aortic graft was utilized to transfer the inferior vena cava from the right to the left atrium without occluding it for any length of time. A description of the operative procedure follows.

A posterolateral thoracotomy is performed through the right fifth intercostal space, and the right pulmonary artery, right pulmonary veins, right main-stem bronchus, and inferior vena cava are dissected free (Fig. 1, *A* and *B*). The lateral aspect of the right atrium is also exposed. Care is exercised to preserve the integrity of the right phrenic nerve. After confirmation of the diagnosis, the right pulmonary artery is examined in order to determine whether or not there is pulmonary valvular stenosis. If there is any doubt, pressure in the pulmonary artery is obtained. If the pressure is over 200 mm. of water, the procedure being described is performed. If the pressure is under 200 mm. of water, a shunt operation is done, since the basic objective is then a matter of supplying more blood to the lung. Assuming that the pressure in the pulmonary artery is more than 200 mm. of water the following maneuvers are then completed.

From the Otho S. A. Sprague Memorial Laboratory, Children's Memorial Hospital, Chicago, Ill.

Supported by funds from the Chicago Heart Association and Grant #8489—B, Department of Health, Education and Welfare, Public Health Service, National Institutes of Health, Bethesda 14, Md.

Read at the Thirty-seventh Annual Meeting of The American Association for Thoracic Surgery at Chicago, Ill., May 4-7, 1957.

A curved coaretation clamp is applied to the lateral aspect of the inferior vena cava, in such a way that blood flow from the inferior vena cava is not impeded (Fig. 1, *B*). An incision is made in the excluded lip of the cava, and a homologous aortic graft is anastomosed to the cava, utilizing a continuous 5-0 arterial silk suture (Fig. 1, *C*). The right pulmonary artery and the right main bronchus are then occluded with umbilical tapes, in order to prevent congestion to the right lung during the remaining maneuvers (Fig. 1, *D*).

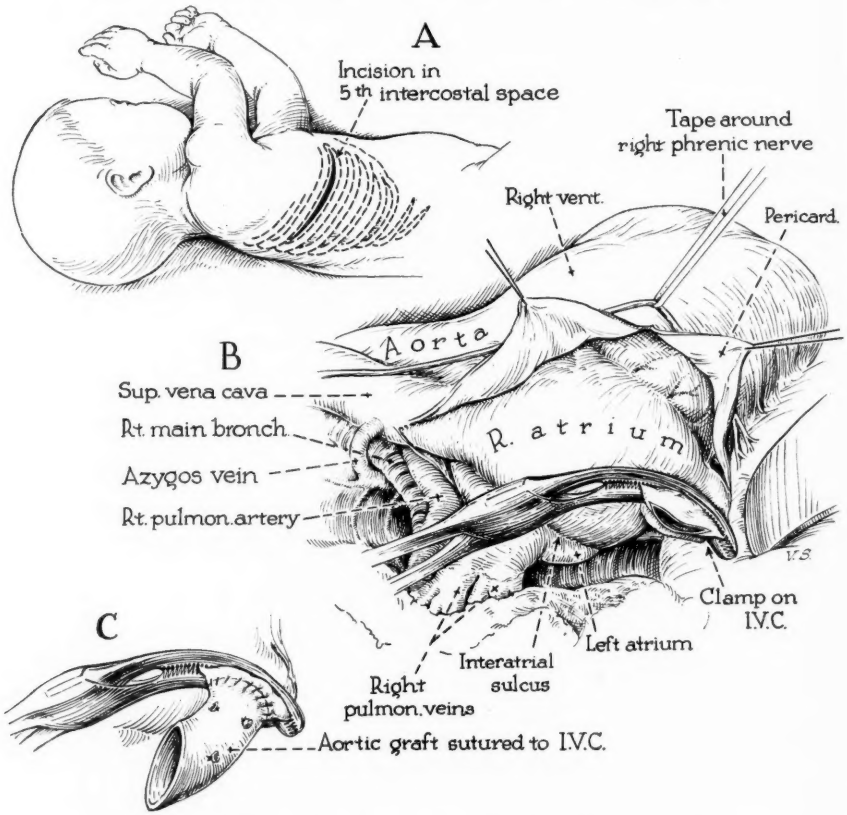

Fig. 1.—*Transplantation of the Inferior Vena Cava and Right Pulmonary Veins.* *A*, A curved posterolateral incision is made through fifth intercostal space.

B, After all the necessary structures are dissected free, a curved coaretation clamp is applied to the lateral aspect of the inferior vena cava to exclude part of its wall without occluding its blood flow to the right atrium.

C, An incision is made in the excluded lip of the inferior vena cava and a homologous aortic graft is anastomosed to it, utilizing continuous 5-0 arterial silk. It is preferable to anastomose segments of the aortic arch because of their thick elastic tissue and their intrinsic curvature.

A coaretation clamp is applied to the base of the right pulmonary veins allowing them to be severed from the left atrium with a common pedicle, and the opposite end of the homologous aortic graft is then anastomosed to the left

atrial stump of the right pulmonary veins. The distal end of the right pulmonary veins is anastomosed to the lateral aspect of the right atrium. A curved coarctation clamp is applied to the right atrium in order to exclude part of its wall for that purpose. Continuous 5-0 arterial silk suture is used for both of these anastomoses (Fig. 1, *E* and 1, *F*).

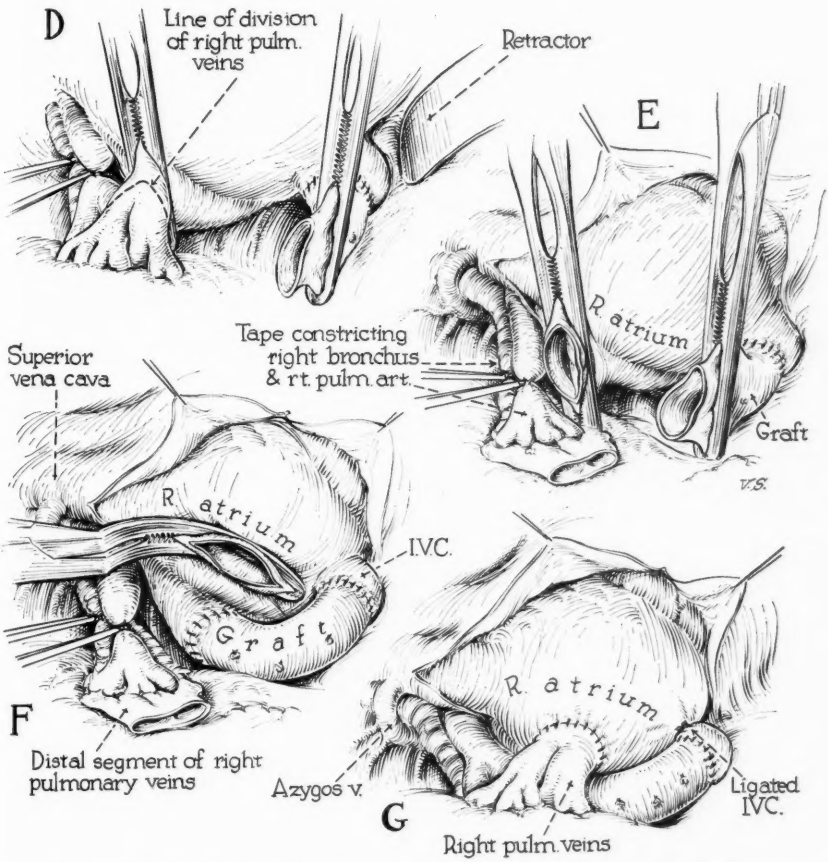

Fig. 1.—Cont'd. *D*, The right pulmonary artery and the right main bronchus with the bronchial arteries are occluded with umbilical tapes. The right pulmonary veins are divided off the left atrium with a common pedicle. Note that a coarctation clamp is not placed on the pulmonary veins. They are left open to allow drainage of any blood that accumulates in the right lung during occlusion.

F, The opposite end of the homograft is then anastomosed to the left atrial stump of the right pulmonary veins. A curved coarctation clamp is applied to the lateral aspect of the right atrium, excluding part of its wall. An incision is made in the excluded portion of the right atrium.

G, The distal stump of the right pulmonary veins is anastomosed to the excluded wall of the right atrium. The occluding tapes are removed from the pulmonary artery and the bronchus and the patient is permitted to adjust to the new circulation. A No. 1 silk ligature is then placed about the point of entry of the inferior vena cava to the right atrium, making flow of blood obligatory from the inferior vena cava through the graft to the left atrium. Note that all of these anastomoses are done by simple over-and-over suture technique utilizing 5-0 arterial silk suture.

The temporary umbilical tape ligatures are removed from the right pulmonary artery and the right main bronchus, and the right lung is aerated. After the patient has had a few minutes to adjust to the new circulation, a No. 1 silk ligature is placed around the point of entry of the inferior vena cava into the right atrium, making flow of blood obligatory from the inferior vena cava through the aortic graft into the left atrium (Fig. 1, *G*). The pericardium is repaired, endothoracic drainage is provided, and the thoracic incision is closed.

Incidentally, in about one third of the operations done in this series, the inferior vena cava was divided from the right atrium,[6] instead of being ligated as described above. Division is now used only if the graft from the inferior vena cava to the left atrium is kinked significantly. Use of segments of the aortic arch, with its thick elastic wall and its intrinsic curvature, has virtually eliminated kinking. By avoiding the need for dividing the inferior vena cava from the right atrium, the operating time for this procedure is greatly decreased.

Of 38 patients operated upon by this method, 15 died in the immediate postoperative period, an operative mortality of 39.5 per cent (Table I). Twenty-three patients survived the procedure and were discharged from the hospital. Four of the survivors died after leaving the hospital, 2 of infectious processes and 2 of pulmonary arteriosclerosis. The remaining 19 patients had very satisfactory alleviation of their symptoms. Most of them had preoperative peripheral oxygen saturations ranging from 35 per cent to 60 per cent of capacity. Postoperatively, they demonstrated increases in peripheral oxygen saturation of 35 per cent to 50 per cent, their levels rising to ranges between 85 per cent and 92 per cent of capacity. Clinically, they demonstrated no cyanosis at rest and had only slight blueness of the lips and nail beds after exercise. They also demonstrated marked increase in exercise tolerance and visible increase in muscle mass of the thighs and calves. Those who had suffered from episodes of syncope, no longer had those attacks. Mental alertness was notably increased. Those who had hepatic enlargement and ascites before operation had recession of the liver and disappearance of the ascites.

TABLE I. OPERATIVE MORTALITY IN TRANSPOSITION OF THE GREAT VESSELS

	TOTAL CASES	SURVIVORS	OPERATIVE DEATHS	MORTALITY RATE (%)
Venous transplants	38	23	15	39.5
Shunt operations	6	5	1	16.7
Totals	44	28	16	36.0

The youngest patient surviving this operation was 6 weeks of age. The oldest was 12 years. This series of 38 patients represents no selection of operative cases on the basis of risk. All patients with transposition of the great vessels who presented themselves for surgery were operated upon, provided they could be reasonably prepared for operation. One third of these patients had had episodes of syncope or actual cerebrovascular paralysis before operation, and another third had had history of congestive failure, yet these were not denied surgery. Only 1 patient with transposition of the great vessels, who

came to the Children's Memorial Hospital for operation, was refused. This was a 4-year-old girl who could not be gotten out of heart failure in spite of 6 weeks of intensive therapy. She remained orthopneic in an oxygen tent, and continued to have severe ascites. She was finally discharged from the hospital on conservative therapy, and died 2 weeks later.

PATHOLOGY OF TRANSPOSITION OF THE GREAT VESSELS

As more and more cases of transpositions were observed, it became increasingly apparent that use of the word "transposition" as an all-inclusive term was misleading. Many varieties exist. Transposition of the great vessels is a type of localized situs inversus deformity in which the aortic-pulmonary septum that divides the embryonic truncus fails to spiral. As a result, unoxygenated systemic blood returning to the right atrium is transported back to the periphery via the aorta. Oxygenated blood returning from the lungs, instead of going to the periphery, is transported back to the lungs by way of the pulmonary artery. The deformity, however, does not end there. Other congenital defects encountered in hearts with normal relationship of the aorta and pulmonary artery are superimposed. For example, most cases of "simple" transposition included patent ductus arteriosus, interventricular septal defects, or interatrial septal defects which permitted the patient to survive for a short while. In addition, transposition of the great vessels has been found associated with right aortic arch, pulmonary valvular stenosis, coaretation of the aorta, tricuspid valve stenosis, isolated dextrocardia, aortic valve stenosis, mitral valve stenosis, and infundibular stenosis. In short, an entirely variable collection of congenital cardiac anomalies may be encountered—all superimposed on the basic defect of transposition of the aorta and pulmonary artery.

In order to clarify the pathology of transpositions, 75 autopsy specimens of this disease, available at the Children's Memorial Hospital, were studied. Five general groups of transposition were finally identified (Table II).

TABLE II. PATHOLOGY OF TRANSPOSITION OF THE GREAT VESSELS

	CASES	PER CENT
Simple transpositions	46	61.3
Transpositions with coarctation of the aorta	11	14.7
Transposition with isolated dextrocardia	1	1.3
Transpositions with pulmonary valvular stenosis	12	16.0
Transpositions with tricuspid valvular stenosis	5	6.7
Total autopsied cases	75	100.0

1. *Simple Transposition of the Great Vessels.*—Forty-six specimens (61.3 per cent of the autopsied cases) had transposition of the great vessels without obstruction to blood flow resulting from other superimposed congenital cardiac anomalies. No chamber deformities, no coaretations, and no valvular stenoses were encountered. Thirty-two had significant patent ductus arteriosus, interventricular septal defects, interatrial septal defects or combinations of these

communications between the right and left sides of the heart. The remaining 14 had histories suggesting closure of a patent ductus arteriosus or patent foramen ovale just before death.

2. *Transposition With Coarctation of the Aorta.*—Eleven specimens (14.7 per cent of the autopsied cases) had transposition of the great vessels in conjunction with coarctation of the aorta. In 10, the coarctation was infantile. One had the adult type. Two specimens also had stenosis of the mitral valve. One infantile coarctation had an associated aortic valvular stenosis with complete hypoplasia of the aortic arch.

3. *Transposition With Isolated Dextrocardia.*—One specimen (1.3 per cent of the autopsied cases) had a functional transposition of the great vessels in association with isolated dextrocardia. This case was of extreme interest because isolated dextrocardias are frequently regarded as forms of "corrected" transpositions, in which not only the arteries, but also the veins entering the heart are transposed. In this particular specimen, the veins had failed to follow the situs inversus deformity in the heart, so that the pulmonary and systemic circulations had become separated.

4. *Transpositions With Pulmonary Valvular Stenosis.*—Twelve specimens (16.0 per cent of the autopsied cases) had significant stenosis of the pulmonary valve. Six had bicuspid pulmonary valves, 5 had morphologic valvular stenosis, and 1 had complete valvular atresia. One case had infundibular stenosis in addition to the pulmonary valvular stenosis. All had interventricular septal defects. Some also had patent ductus arteriosis or interatrial septal defects. In 3 specimens the interventricular septal defect was so large that the ventricles functioned as a single chamber in which extensive mixing of systemic and pulmonary blood occurred. In the remaining 9 cases, the interventricular septal defect was small, but seemed functionally significant.

5. *Transposition With Tricuspid Valvular Stenosis.*—Five specimens (6.7 per cent of the autopsied cases) had transposition of the great vessels together with tricuspid valvular stenosis or atresia. Three also had pulmonary valvular stenosis. All had interatrial and interventricular septal defects that probably allowed considerable mixing of the systemic and pulmonary circulations.

It was apparent that all transpositions could not be managed alike. Most of them (e.g., the first three groups described) were amenable to partial correction by transplantation of the right pulmonary veins and the inferior vena cava. However, those with stenosis of the tricuspid valve or with significant pulmonary stenosis were basically problems in increasing the flow of blood to the lungs and were candidates for shunt operations. It was decided that those patients having pressures in the pulmonary artery over 200 mm. of water would be treated by partially transplanting the venous return to the heart. Those with pressures less than 200 mm. of water would be treated by aortic-pulmonary or subclavian-pulmonary anastomosis.

Incidentally, 6 patients fell into the latter category and they should be summarized, although they do not constitute the major subject of this report.

One of them had transposition associated with tricuspid atresia and 5 had transposition associated with pulmonary valvular stenosis. Two were diagnosed preoperatively and had left aortic-pulmonary anastomoses. The remaining 4 had right thoracotomy in preparation for transplantation of the right pulmonary veins and the inferior vena cava, when pressures less than 200 mm. were unexpectedly encountered in the pulmonary artery. Right subclavian-pulmonary anastomoses were performed. One of the 6 patients with shunt operations died in the immediate postoperative period, an operative mortality of 16.7 per cent (see Table I). The surviving patients had satisfactory alleviation of their cyanosis and other clinical symptoms.

ANALYSIS OF DEATHS FOLLOWING OPERATION

The patients dying after transplantation of the right pulmonary veins and the inferior vena cava fell into two categories. Fifteen died during surgery or in the immediate postoperative period of causes unrelated to the operative procedure. Four died after being discharged from the hospital.

1. *Immediate Operative Deaths.*—Of the 15 operative deaths, 8 were, in all probability, secondary to the patient's disease and were unavoidable. The remaining 7 resulted from technical difficulties during or immediately after operation and represent deaths which might be prevented in the future (Table III).

TABLE III. ANALYSIS OF DEATHS FOLLOWING OPERATION

Immediate Operative Deaths	
1. Cardiac failure	5
2. Cerebrovascular accidents	3
3. Hemorrhage from right lung	2
4. Right pulmonary edema with anoxia	2
5. Intercostal hemorrhage	1
6. Supraventricular tachycardia	1
7. Digitalis escape	1
Delayed Deaths	
1. Diarrhea	1
2. Pulmonary arteriolar sclerosis	2
3. Bronchopneumonia	1

The unavoidable operative deaths occurred in two ways. Three patients died of cerebral anoxia, never regaining consciousness in the postoperative period. Five patients died from various types of cardiac failure. One of these, who had had two previous episodes of cardiac failure, developed cardiac dilatation and asystole during operation. Another developed intractable ventricular fibrillation during surgery. Two others died in the first postoperative day with bilateral pulmonary edema and enlarged liver. The fifth patient died, 9 days postoperatively, of right ventricular failure—demonstrating distention of the superior vena cava and unilateral right pulmonary edema.

The 7 preventable deaths were related to inadequate control during surgery of the increased pressure in the pulmonary artery, or resulted from difficulties in postoperative care. Four were in the former category. One, early in the series, died of severe hemorrhage into the tracheobronchial tree.

The pulmonary artery had been occluded, but the bronchus and bronchial arteries had been left open. Apparently, the bronchial arteries had dilated as a compensatory mechanism for the transposition and, during the half hour of occlusion of the right pulmonary veins, needed to transfer them to the right atrium, the lung became filled with blood. This blood extravasated into the pulmonary alveoli and interfered with respiration. Two other deaths, occurring in infants, were characterized by the appearance of small amounts of hemorrhagic frothy sputum in the trachebronchial tree early during the operative procedure. This did not seem alarming at the time, but it apparently produced enough postoperative pulmonary edema to reduce the infants' lung function to dangerous levels. The infants died of anoxia in the immediate postoperative period. The fourth death from pulmonary complications occurred in a 3-year-old patient who was a satisfactory operative risk and who tolerated the operative procedure well. Manipulation of the lung to return it to the pleural cavity, however, resulted in rupture of the pulmonary capillaries and severe pulmonary hemorrhage. Apparently, chronic hepatic anoxia had produced some obscure type of interference with blood coagulability and the hemorrhage continued until the patient died.

This experience emphasized the importance of early occlusion, during operation of the bronchial arteries as well as the pulmonary artery. Since introduction of these precautionary manuevers, pulmonary complications have decreased.

The last 3 preventable deaths were related to postoperative care. In one patient, a bleeding point in an intercostal vein was not detected during the operative procedure, because cooling the patient had caused reduction in blood flow. Hemorrhage occurred in the postoperative period and it was not detected in time to save the infant's life. In another patient, the body temperature drifted, during operative cooling, to very low levels. Supraventricular tachycardia resulted and several hours elapsed before this abnormal rhythm could be corrected. By that time, the heart was exhausted and the patient ultimately died of cardiac failure. The final death followed use of a short-acting digitalis preparation to sustain an infant's failing heart during the operative and postoperative period. Since the digitalis was excreted rapidly, its effect was dissipated by the end of the first postoperative day. In ensuing attempts to restore digitalization, the patient had several episodes of restoration of cardiac function followed by pulmonary edema, and finally died. It is impossible to say with certainty whether or not the patient's heart failed in spite of digitalis. However, we have since adopted use of long-acting digitalis preparations and feel that smoother cardiac support has been obtained during the critical immediate postoperative period.

2. *Delayed Deaths.*—Four patients survived the immediate postoperative period and were discharged from the hospital. They died of causes unrelated to the operative procedure. Two patients died of severe infections—one of diarrhea, the other of bronchopneumonia. The remaining 2 delayed deaths

resulted from pulmonary arteriosclerosis. Actually, their ultimate fatal outcome might have been predicted from their response to the operative procedure. They did not show the usual alleviation of cyanosis, although they recovered from the operative trauma. Several weeks later, they died suddenly and without apparent cause. Autopsy revealed severe pulmonary arteriosclerosis.

FATE OF THE HOMOGRAFTS USED FOR TRANSFERRING THE INFERIOR VENA CAVA

An interesting and important problem concerns the ultimate fate of the homologous aortic grafts utilized to transfer the inferior vena cava from the right to the left atrium. The longest follow-up of these grafts in patients in our series has been 26 months. Although they show signs of calcification of the wall during this period, none have clotted or ruptured. In fact, they seem to be doing an excellent job of conducting the blood flow of the inferior vena cava to the left atrium. Unfortunately, they do not grow. To compensate, we introduce as large a graft as possible during the operative procedure. Grafts not less than 1.0 cm. in diameter are desired, regardless of the age of the patient at the time of operation. In addition, the azygos vein is left intact, so that, should any relative obstruction of the inferior vena cave occur with growth of the patient, there would be available collateral circulation to prevent the formation of hepatic congestion or ascites.

Incidentally, a dozen homologous aortic grafts were introduced in dogs, from the inferior vena cava to the right atrium, and were followed for over 3 years. Some were introduced in puppies that have since grown to four or six times their original weight. These grafts have recently been examined and show excellent function.

SECOND-STAGE PROCEDURE TO COMPLETE THE CORRECTION OF TRANSPOSITION OF THE GREAT VESSELS

Although none of the surviving patients show recurrence of cyanosis, a great deal of thought has been devoted to the development of a second-stage procedure which might permit transplantation of the superior vena cava and the left pulmonary veins—thus completing the correction of the transposition anomaly. Fig. 2 demonstrates our current theoretical approach to that problem. A description is included in the legend. This procedure has not been performed on human beings, but a number of studies have been done in the animal laboratory and the morgue which demonstrates its feasibility.

Several grafts were introduced, in acute dog experiments, between the end of the left innominate vein and the left auricle. When the grafts were short and the shunt was obligatory, the grafts did not clot. This was also attempted in one human being in conjunction with earlier experiments on transpositions. Although the patient died during the first postoperative day, the graft between the innominate vein and the left atrium remained patent. Unfortunately, it has not been possible to determine whether occlusion of the origin of the left innominate vein would have detrimental long-term results. However, if this proves to be the case, the graft could be introduced by end-to-side anastomosis to the left innominate vein.

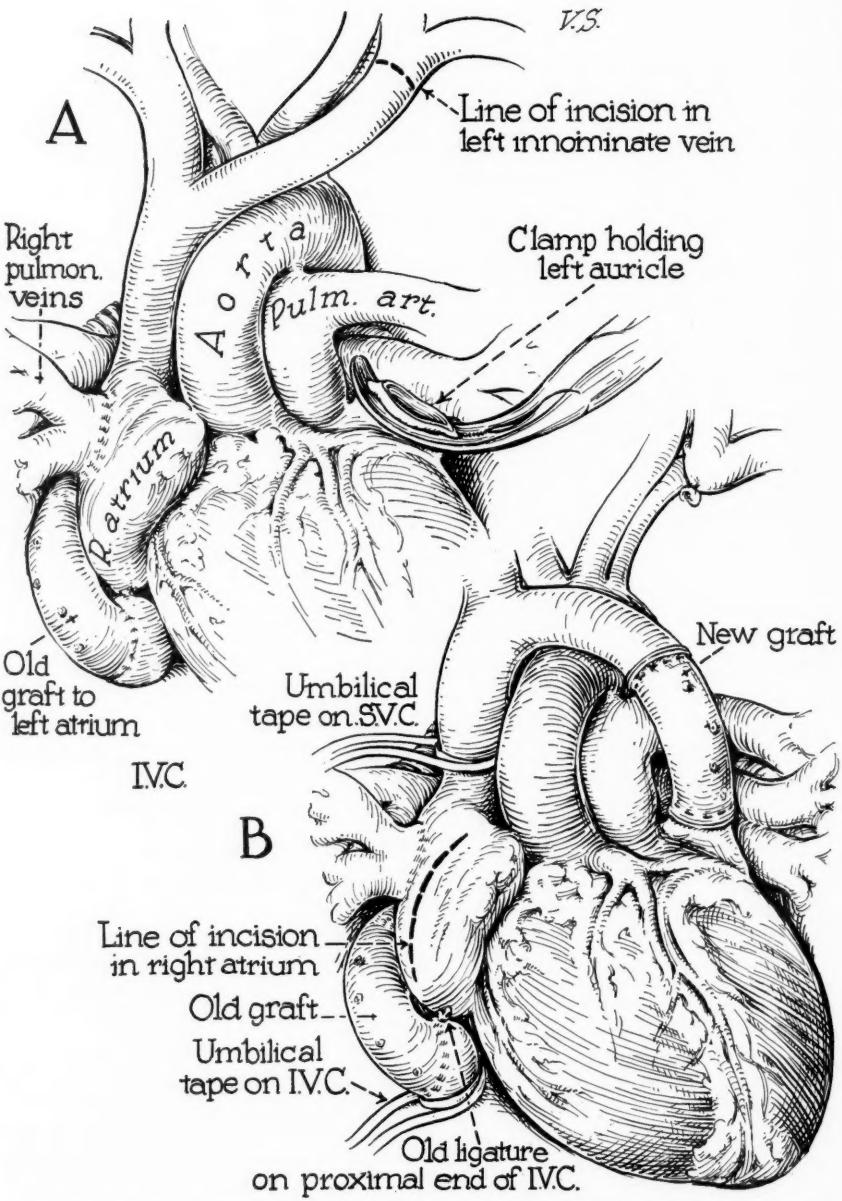

Fig. 2.—***Second-Stage Procedure or Completing the Correction of Transposition of the Great Vessels.*** The patient is supported by extracorporeal circulation or is under hypothermia.

A, The left innominate vein, the superior vena cava, and inferior vena cava, the left auricle and the lateral aspect of the right atrium are exposed. A curved coarctation clamp is applied to the base of the left auricle and the auricular tip is amputated.

B, An homologous aortic graft is utilized to connect the distal end of the left innominate vein to the open tip of the left auricle. A curved bulldog clamp is then reapplied to occlude the base of the left auricle. It is not shown for the sake of simplicity. Umbilical tapes are applied about the venae cavae in preparation for inflow occlusion of the heart.

In addition, 8 dogs have had incision of the interatrial septum during hypothermia, as shown in Fig. 2. None have developed signs of heart block—a finding which has occurred on several occasions when a circumferential incision is made in the interatrial septum in attempts to transfer the systemic and pulmonic circulations by internally shifting the septum.

Finally, the invagination of the left pulmonary veins into an incision in the interatrial septum has been performed in a number of dogs without definite

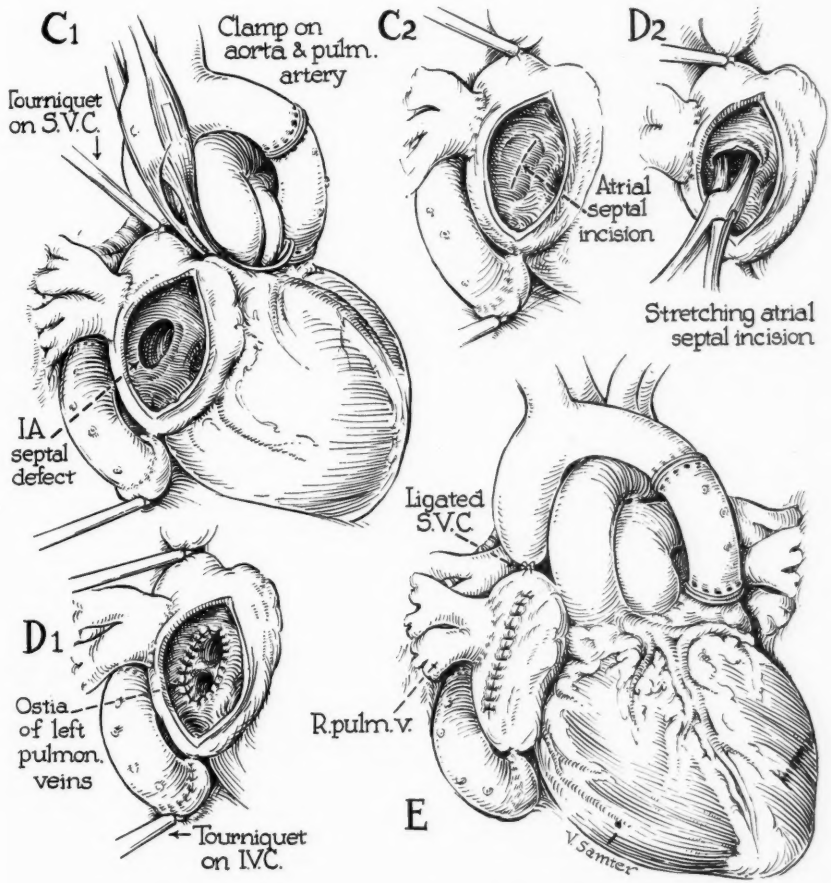

Fig. 2.—Cont'd. *C1*, After inflow occlusion a clamp is placed about the base of the aorta and pulmonary artery and the right atrium is opened.

D1, If an interatrial septal defect is present the ostia of the left pulmonary veins are anastomosed to the rim of the defect, using 5-0 arterial silk sutures.

E, The incision in the right atrium is repaired and the inflow occlusion is released. After the patient has adjusted to the new circulation, a ligature is placed about the base of the superior vena cava, making flow of blood through the graft into the left atrium obligatory.

C2, If no septal defect is present, a small incision is made parallel to the edge of the tricuspid valve.

D2, The incision is then stretched to proper size with a curved hemostat. The ostia of the left pulmonary veins are then sewn to the edge of the incision in the same manner as shown in *D1* and the operation is completed as previously described for *E*.

anatomic evidence of occlusion of the ostia of the right pulmonary veins. Recently, the second-stage procedure was performed on a patient with transposition who had just died following transplantation of the inferior vena cava and the right pulmonary veins. Fluid was introduced into the abdominal portion of the inferior vena cave and a water manometer was used to see if the venous pressure was increased. So far as could be determined, free flow of fluid occurred through the inferior vena cava into the left atrium. There was no significant obstruction caused by the invagination of the left pulmonary veins.

It is emphasized that this second stage (Fig. 2) is entirely theoretical and, with the exception of the observations above, remains entirely unproved. It is presented merely to show in what direction our present efforts are turned.

COMBINED OPERATION FOR CORRECTING TRANSPOSITIONS

The logical end point of this line of reasoning is combination of the first- and second-stage operations into a single procedure for completely correcting transposition of the aorta and pulmonary artery. This would require support of the patient by extracorporeal circulation during the time needed to complete the operation. Although the details have been worked out theoretically, the combined procedure remains entirely untested and unproved. However, the proposed operation may be summarized in the following paragraph.

Part of the transfer of the venae cavae (i.e., transfer of the superior vena cava by introducing a homologous aortic graft between the left innominate vein and the left auricle as shown in Fig. 2) could be done before the patient was placed on extracorporeal circulation. After extracorporeal circulation was started, the right pulmonary veins would be divided from the left atrium with a common pedicle (see Fig. 1,*D*). The inferior vena cava would be divided from the base of the right atrium between clamps, and the distal end of the cava would be anastomosed to the left atrial stump of the right pulmonary veins. The right atrium would be opened, the atrial wall would be incised if necessary, and the left pulmonary veins would be invaginated and anastomosed to the opening in the septal wall of the right atrium (Fig. 2, D_1). The distal end of the right pulmonary veins would then be anastomosed to the incision in the lateral wall of the right atrium. If the patient's condition permitted, the ventricle could be opened and an interventricular septal defect could be repaired after completion of the above maneuvers. If a ductus were present it might also be ligated. This would complete the correction of transposition of the great vessels, including elimination of all shunts between the right and left sides of the heart.

SUMMARY

1. An operative procedure for transplanting the right pulmonary veins and the inferior vena cava, thereby partially correcting transposition of all aorta and pulmonary artery, is described.

2. Clinical application of this procedure to 38 patients is summarized. The operative mortality was 39.5 per cent. Four patients died after leaving

the hospital of causes unrelated to the operation. The remaining 19 survivors had very good clinical postoperative results.

3. Many types of transposition anomalies exist. Not all of them are amenable to this procedure. The varieties of transposition are described and the indications for this operation are given. Treatment of some transpositions by shunt operation is summarized.

4. The causes of death following partial correction of transposition of the great vessels are described in detail. Means of prevention are emphasized.

5. Long range animal studies regarding the fate of the homologous aortic grafts used to transplant the inferior vena cava are related.

6. A proposed second-stage operation making possible completion of correction of transposition of the great vessels is described. Experiments demonstrating its feasibility are enumerated.

7. A theoretical combined operation, permitting complete correction of transposition in one stage under extracorporeal circulation, is described.

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DISCUSSION

DR. WILLIS J. POTTS, Chicago, Ill.—It is a pleasure to endorse the work which Dr. Baffes has presented this afternoon. A number of years ago he said, "I am going to whip the problem of transposition of the great vessels." I will say that he and Dr. De Boer and Dr. Riker have given it a good threshing, although they have not beaten it into complete submission. The operation, though far from perfect, appears to be the best we have to offer at the moment. Considering the fact that these children are all in rather desperate condition, many having been in heart failure, the mortality is not too prohibitive. How long the surviving children will live and what their future will be, is, of course, unknown. The amazing thing is to see what the child will tolerate. It is the same with this operation as with many other operations—how will they hold up over a period of years? I cannot help but say this: parents of helpless children grasp at straws, and all the surgical profession can do is to offer them the best we have today and anticipate that further research and study will provide better procedures tomorrow.

What always amazes me is the gratitude of the parents for any help they receive for their unfortunate children. I sometimes think they have a more balanced attitude toward new procedures than we have. Parents are grateful for help and not bitter or resentful when the outcome is unfortunate. We have all had this experience, I am sure, after an unfortunate outcome. The parents say, "Doctor, we know you have done your best and we

don't hold it against you that there has been a misfortune with our child." Such an attitude is probably the greatest stimulus to renewed efforts, and we hope after the laboratory tests to review the procedure again and if possible try it on another child. Transposition of the great vessels requires much more work. Some day someone will figure out a better operation and that is the way it should be. Many fine operations have to give way before improved methods.

DR. EARLE B. KAY, Cleveland, Ohio.—I should like to compliment Dr. Baffes and his colleagues on such an outstanding paper. I am sure that all of us who have been interested in this subject have encountered the same problem. Certainly their results have been the best to date.

I would like to discuss two aspects of transposition of the great vessels; first, the technical aspect of surgical correction, and second, the physiologic aspect of the associated pulmonary hypertension. We first attempted to solve this problem by various shunt operations. Later we performed aorta-pulmonary artery re-anastomoses. All of the 3 patients, as previously reported, died within 4 to 6 hours postoperatively from pulmonary edema and multiple petechial pulmonary hemorrhages as a result of transposing the dominant hypertrophied right ventricle into the pulmonary system, which was already affected by the pulmonary hypertension as seen in these patients. To be successful, we felt that any re-channeling of blood flow would have to be accomplished on the inflow rather than the outflow side of the heart. Because it is impossible to correct (completely) the venous inflow by partial vena caval pulmonary vein transplants, we attempted in the laboratory to re-channel (completely) the venous inflow at the atrial level by the following technique.

(slide) A longitudinal incision is made in the lateral wall of the right auricle along the projected course of the superior vena cava. This incision fashions a "U" flap approximately 1 inch in width just proximal to the opening of the inferior vena cava. The auricular septum is then exposed. Two large openings are then made in the septum utilizing the entire septum except for a narrow anteroposterior strip of septal tissue which separates the two openings. The superior vena cava is reconstructed down to the "U" flap by suturing the lateral wall of the auricle to the posterior base of the auricular septum. The "U" flap is then sutured circumferentially, about the stoma closest to the tricuspid valve, in such a manner as to include the stoma of the coronary sinus. This maneuver diverts all of the vena caval blood to the left auricle.

(slide) The lateral wall of the left auricle on the vaivular side of the pulmonary veins is then grasped by forceps and brought to the septal division where it is sutured to the bridge of atrial septum as well as the cephalad side of the "U" flap. This diverts all of the pulmonary venous drainage to the remaining portion of the right auricle. The right auricular chamber is then reconstructed by suturing the anterior segment of the lateral wall of the right auricle resulting from the initial incision to the reconstructed vena cava.

The operation is performed by means of extracorporeal circulation, utilizing a pump-oxygenator. Other defects, such as an associated ventricular septal defect, may be corrected at the same time.

(slide) Two children, one 3 years old and the second 18 months old, have now been operated upon using this technique. Neither of the infants survived. The 18-month-old baby weighed only 11 pounds and was an extremely poor operative risk. He died 6 hours postoperatively from total atelectasis of the left lung. The 3-year-old died 36 hours postoperatively from increasing failure from a heart block. In neither case was there any evidence of pulmonary edema or petechial pulmonary hemorrhages, as had been present in patients having arterial transplantations.

This brings up the second aspect of the problem—that of pulmonary hypertension. Detailed examinations of the pulmonary vasculature in patients with transposition of the great vessels by our pathologist, Dr. John MacKrell, has shown varying degrees of internal and medial sclerosis beginning at about the age of 6 months, and becoming more severe both as to the degree and extent of vessels involved with increasing age.

(slide) This represents the pulmonary vasculature (small arteries and arterioles) of a 5-week-old baby. The media is more thick than what one sees in normal lungs of babies of this age. Other vessels appeared normal.

(slide) This represents the pulmonary vasculature in a 7-month-old baby which shows some medial thickening and slight intimal proliferation. These changes were spotty throughout the lung. Other vessels were fairly normal.

(slide) This slide represents the changes seen at 11 months of age. The intimal proliferation is greater with resulting reduction in the size of the vessel lumen.

(slide) At 18 months of age these changes are even more severe and the number of vessels involved is greater.

(slide) This slide represents the pulmonary vasculature of the 3-year-old patient who was operated upon. One can note almost complete loss of vascular lumen from the extensive intimal proliferation.

From the above studies, we have gained the impression that such children would most likely survive operation if they could be operated upon before such severe degrees of pulmonary vascular sclerosis developed. I would like to ask Dr. Baffes to comment on the age distribution of his patients as to the mortality of operation and the benefit from operation at the various ages.

DR. JOHN E. JESSEPH, Seattle, Wash.—These remarks are made for Dr. K. Alvin Merendino of the Department of Surgery of the University of Washington, who was unable to attend this meeting. Our interest in this problem has been in large part stimulated by the efforts of Dr. Baffes and his group and we wish to extend our congratulations to them for the excellence of their presentation. Our interest, however, has centered in a one-stage procedure for the total correction of transposition through the intracardiac route, using the pump-oxygenator and induced cardiac arrest.

(slide) These diagrams illustrate the situation which occurs in a typical transposition of the great vessels, the aorta arising from the right cardiac ventricle. Here is shown, schematically, the installation of a molded, curved, Ivalon prosthetic interatrial septum, which is placed so that it lies through an artificially created interatrial septal defect, or an enlarged septal defect if one is already present.

(slide) Here is a similar diagram showing the course of blood in a typical uncorrected transposition with desaturated blood coursing out of the arterial vessels. Following installation of the prosthesis, there is complete correction so that there is bidirectional shunting of venous inflow to the heart, with the result that pulmonary inflow is directed to the right atrium and out the pulmonary vessels on the left.

(slide) This is a section taken at the A-V level to show another view of the prosthesis, and indicating pulmonary venous blood passing through the saddle of the prosthesis across into the right ventricle, with systemic venous blood from below in this case.

(slide) This is an A-P view of what was shown in the first diagram of this molded Ivalon prosthesis.

This method has been employed in 2 cases. Unfortunately both patients died in the immediate postoperative period, the first because it was impossible to resuscitate the heart following arrest; the second died about 5 hours postoperatively, after having a normal immediate period, when turned on her right side. She died a respiratory death, and at autopsy the impression was that she had embolized air trapped in the heart at the time of the procedure. These operations done so recently have only strengthened our conviction that this sort of problem is best handled by this sort of direct, open, one-stage procedure.

DR. WILLIAM H. MULLER, Jr., Charlottesville, Va.—I should like to congratulate Dr. Baffes and his associates on their excellent results in dealing with this very difficult problem. We became interested in it some 4 or 5 years ago at the UCLA Medical School, and operated on about 14 patients, in whom we transposed the superior vena cava and the right pulmonary veins. Only 3 of those patients survived for a period longer than one week. One did survive for 3 months and obtained considerable improvement, but most of these

seemed to die because of some difficulty with the central nervous system. In examining these specimens at post-mortem examination, we did not believe that we had compression of the superior vena cava by these pulmonary veins as Dr. Baffes implied.

(slide) This is the post-mortem examination, with both pulmonary veins implanted into the right auricle. The superior vena cava is implanted in the pulmonary vein stump and cannot be visualized.

(slide) We have attempted to transpose the pulmonary venous return to the right ventricle by placing an Ivalon patch so that blood flow is directed from the pulmonary veins to the tricuspid valve. More recently, we have molded an Ivalon sponge sheet so that it fits about these structures much better. In carrying out this procedure, it is necessary to excise the entire auricular septum and, in addition, to enlarge both auricles in the area of the septum so that atrial blood flow may occur in both directions. This is done by extending the incision in the auricular wall superiorly into the transverse cardiac sinus and suturing in the incision at the point which passes through the septum, a diamond-shaped Ivalon sponge patch.

DR. THOMAS G. BAFFES, Chicago, Ill. (Closing).—I wish to thank the discussants very much for their remarks. I would just like to say that the logical end point of this procedure is a combination of the two stages which were presented. Such a combined procedure, utilizing extracorporeal circulation, is in the blueprint stage at the moment. A brief description of the combined procedure is included in the final paper. It was not presented here because I did not wish to burden a clinical discussion with material which is in the laboratory stage. However, it seems feasible and certainly should be attempted after further trials in the laboratory.

In answer to Dr. Kay's question concerning the age of the patients, 10 were less than 1 year old and 5 were less than 6 months old. The difficulty in operating on those less than 6 months of age is that the homografts will not grow. If one can get the patient to survive beyond 6 months of life before operation, it is possible to put in a graft that is fairly adequate in size. In addition, the azygos vein should be left intact so that, should there be any partial occlusion of the inferior vena cava as the patient grows, there will always be collateral circulation for the blood to get out of the liver and kidneys.

MECHANICAL BY-PASS DURING THORACIC AORTIC CROSS-CLAMPING

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PROLONGED cross-clamping of the thoracic aorta is often followed by paraplegia or death.[1] Several techniques have been developed to protect the patient during this dangerous time interval. Hypothermia[2-7] and various types of intraluminal and extraluminal by-pass shunts have been used.[8-14] None, however, has proved to be ideal and the search for better methods has continued.

In 1951, Leeds and Culiner[15] reported the use of a pump to shunt blood from the carotid to the femoral artery. They were able to cross-clamp the aortas of dogs for 3 hours without damage to the spinal cord. In 1955, Cross and his associates[16] reported an experimental study in which a pump was used to shunt blood from the left subclavian to the femoral artery during cross-clamping of the aorta. They also employed shunts from the left ventricle to the femoral and right innominate artery for excision of the aortic arch. Blood was picked up under 50 mm. Hg negative pressure and taken to a reservoir which was primed with blood. It was then pumped from the reservoir to the femoral artery. Dogs weighing 30 pounds required pump outputs of approximately 500 to 700 c.c. per minute (about 36 to 51 c.c. per kilogram per minute). Femoral artery pressures were maintained higher than 80 mm. Hg. Fourteen dogs survived without neurologic damage. Cooley and DeBakey[17] recently reported a case in which an aneurysm of the ascending aorta was excised with the use of a pump-oxygenator and total cardiorespiratory by-pass. The present paper is concerned with the experimental and clinical use of a mechanical by-pass during cross-clamping of the thoracic aorta.

METHODS

Mongrel dogs were used. They were anesthetized by the intravenous administration of thiopental sodium. Tracheal intubation was carried out and the lungs were rhythmically inflated with oxygen, or oxygen and ether if necessary, by means of a mechanical insufflation apparatus. In some of the animals, two incisions in the left thorax were made, one through the fourth and the other through the ninth or tenth interspace. In others, one long incision through the sixth interspace was employed. In most of the experiments, the aorta was mobilized immediately below the subclavian artery and distally just

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Aided by grants from United States Public Health Service and Indiana Heart Foundation.

Read at the Thirty-seventh Annual Meeting of The American Association for Thoracic Surgery at Chicago, Ill., May 4-7, 1957.

above the diaphragm. It was then occluded with Potts ductus clamps for one hour. In others only the proximal clamp was applied. An attempt was made to estimate blood loss incurred during the operation and blood was replaced, if necessary, in appropriate amounts. In about one half of the operations strict sterile technique was used and, if the animal survived, it was observed for 3 or 4 weeks. In others, aseptic technique was not employed and after a few days many of the survivors developed infections of their wounds. These dogs were then sacrificed. The external jugular vein and the carotid, brachial, and femoral arteries were isolated and cannulated as needed. Pressures were monitored by means of a Statham pressure transducer recording on a Sanborn Twin-Viso Cardiette.

In those animals in which a by-pass was used, heparin was administered in the amount of 2 mg. per kilogram of body weight given intravenously immediately before insertion of the cannulas. Following completion of the procedure, protamine sulfate was administered in the amount of 2 mg. per kilogram

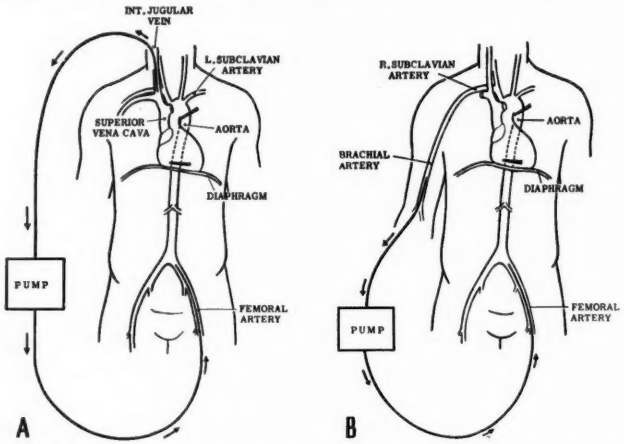

Fig. 1.—Drawings showing the mechanical by-pass unit. In that on the left, blood is removed from the superior vena cava, and in the other, it is taken from the brachial artery. It is led through the pump and into the femoral artery in both.

of body weight. After this a slow drip was given of 5 per cent dextrose and water to which protamine sulfate, 1 to 2 mg. per kilogram of body weight, was added. The mechanical by-pass unit was simple, one Sigmamotor pump, one segment of latex rubber tubing for use as a pumping chamber, and Mayon or Tygon tubing of appropriate size to and from the experimental animal. Plastic or metal cannulas were inserted into the appropriate vessels. The by-pass unit was filled with normal saline solution and the pump was set to the proper speed. The plastic tubing to and from the pump was connected to the catheters in the blood vessels in such a way as to exclude air bubbles. The pump was then turned on shortly before the aorta was clamped. Fig. 1 illustrates the mechanical by-pass unit in operation. The drawing on the left demonstrates the removal of blood from the superior vena cava and that on the right from the

brachial artery. In both, blood goes through the pump into the femoral artery. Preliminary observations of the rate of blood flow through the inferior and superior vena cava during aortic cross-clamping were made. A large plastic catheter was placed in the appropriate cava. The cava was then occluded so that blood flow from it would pass through the catheter (Fig. 2). Blood was led through the plastic tubing to a graduated reservoir which was placed below the dog so that a mild negative pressure would be established when the flow began. A level was maintained in the reservoir by taking blood from it and then pumping it back into a vein of the animal. The blood volume of the dog was thus maintained in a normal state. At intervals the pump was stopped and the length of time taken for the blood level to rise a certain number of milliliters was observed. These data were then converted to blood flow in milliliters per minute or millililiters per kilogram per minute.

In some animals the oxygen saturation of the superior vena caval blood before and during thoracic aortic cross-clamping was measured. The method of Roughton-Scholander was used.

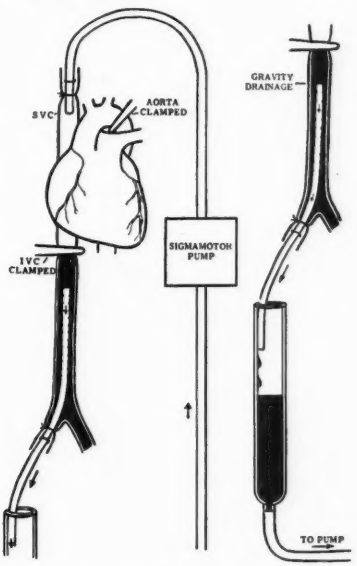

Fig. 2.—Diagram showing the method used for measuring the rate of inferior vena caval blood flow.

EXPERIMENTAL OBSERVATIONS

In a control group of 17 animals, the aorta was occluded just beyond the left subclavian and just above the diaphragm for one hour. One survived without paraplegia, 2 with paraplegia, and 14 died within a few hours after the operation. Some of the animals that died were obviously paraplegic before death (Table I). Most of them exhibited a severe state of shock and many had a bloody diarrhea.

TABLE I. AORTA CLAMPED IMMEDIATELY BELOW BASE OF SUBCLAVIAN ARTERY AND JUST ABOVE DIAPHRAGM

FLOW RATE OF SHUNT IN C.C./KG./MIN.	LIVING WITHOUT PARAPLEGIA	LIVING WITH PARAPLEGIA	DEATH (SOME PARAPLEGIC BEFORE DEATH)	TOTAL
		Control		
0	1	2	14	17
		Aortic By-pass, Superior Vena Cava to Femoral Artery		
20	13	0	1	14
15	1	0	0	1
10	6	0	0	6
5	3	0	0	3
	23	0	1	24
		Aortic By-pass, Brachial to Femoral Artery		
15	8	0	1	9

In another group of 24 animals the thoracic aorta was similarly cross-clamped and a measured by-pass of blood from the superior vena cava was supplied to the femoral artery. The results were quite different. Altogether there were 23 survivors without paraplegia and a single animal died. In 14 of these animals, 20 c.c. per kilogram per minute of blood was shunted. Thirteen of them survived without paraplegia and one died. One animal in which the shunt was 15 c.c. per kilogram per minute survived without paraplegia, and the same was true of all 6 animals in which the flow was 10 c.c. per kilogram per minute and in 3 animals in which the flow was 5 c.c. per kilogram per minute.

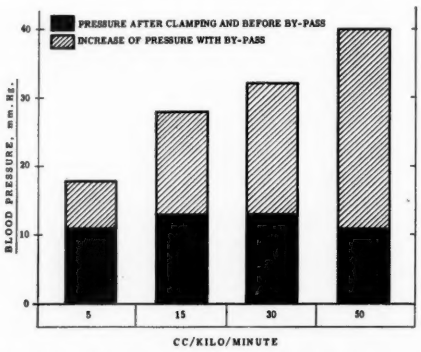

Fig. 3.—Chart of the mean abdominal aortic blood pressure with the descending thoracic aorta occluded with 2 clamps before and after by-pass from brachial to femoral artery at different rates of flow.

The results were similarly good in a group of 9 animals in which the by-pass was from the brachial to the femoral artery during double thoracic aortic cross-clamping. Eight of these dogs survived without paraplegia; one died with a hemothorax 24 hours after operation.

In a number of animals, distal aortic mean blood pressures were observed after cross-clamping the aorta and again after a measured by-pass was instituted (Fig. 3). As soon as the thoracic aorta was doubly cross-clamped the mean distal pressures ranged from 11 to 13 mm. Hg. With 5 c.c. per kilogram per

minute by-passed from the brachial to femoral artery, the distal aortic pressure rose to 15, with 15 c.c. per kilogram per minute to 28, with 30 c.c. per kilogram per minute to 33, and with 50 c.c. per kilogram per minute to 40 mm. Hg. In

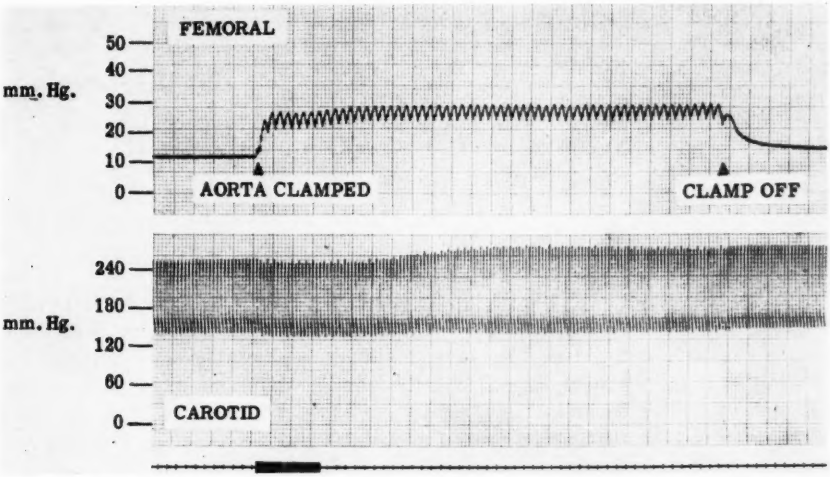

Fig. 4.—Photograph of simultaneous femoral and carotid artery blood pressure tracings in a dog with the descending thoracic aorta occluded with 2 clamps, one below the subclavian and the other above the diaphragm, before, during, and after brachial to femoral artery by-pass shunt at a rate of 15 c.c./Kg./min.

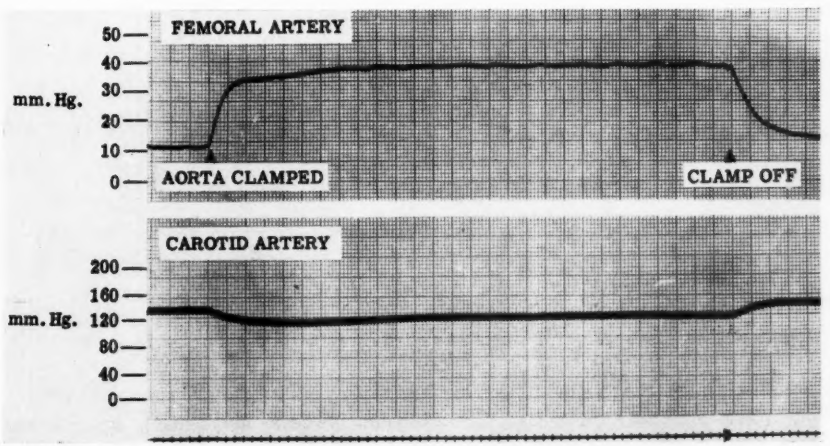

Fig. 5.—Photograph of simultaneous femoral and carotid mean arterial blood pressure tracings in a dog with the descending thoracic aorta occluded with 2 clamps, one below the subclavian and the other just above the diaphragm, before, during, and after brachial to femoral artery by-pass shunt at 50 c.c./Kg./min.

a number of animals, carotid and femoral blood pressures were monitored during aortic cross-clamping and by-pass shunt. With a flow of 15 c.c. per kilogram per minute, the by-pass brought about a significant elevation in the femoral

artery pressure and only a temporary slight depression in carotid artery pressure (Fig. 4). With rates of flow of 50 c.c. per kilogram per minute a greater rise in femoral artery pressure was noted, together with a modest sustained depression of carotid artery pressure (Fig. 5).

TABLE II. BLOOD OXYGEN SATURATION IN PERCENTAGE

SUPERIOR VENA CAVA		CAROTID ARTERY
BEFORE AORTIC CLAMPING	AFTER AORTIC CLAMPING	AFTER AORTIC CLAMPING
56.8	101.0	102.0
64.4	98.1	99.6
---	96.3	99.4
77.7	71.1	100.0
73.3	86.6	95.7
63.0	72.0	88.0
74.3	98.0	110.0

Oxygen saturation of the superior vena caval blood ordinarily rose during aortic cross-clamping (Table II). In four instances the arterial saturation ranged from 96.3 to 101 per cent. In two instances it rose to a less significant degree (72 and 86.6 per cent). In a single animal the saturation actually fell slightly. In one animal, blood flow through the superior vena cava before, during, and after thoracic aortic cross-clamping was measured (Fig. 6). The flow rapidly increased from a rate of about 400 to approximately 1,000 c.c. per minute.

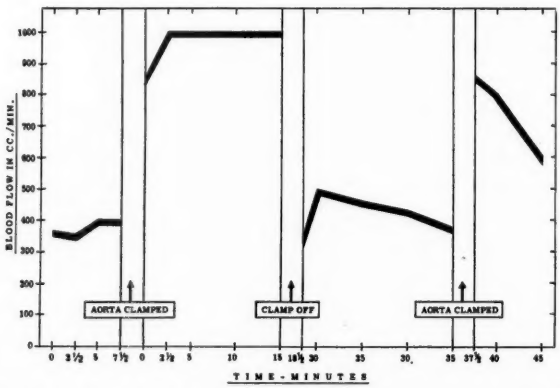

Fig. 6.—Graph of the rate of blood flow from the superior vena cava of a dog before, during, and after cross-clamping the thoracic aorta just below the base of the subclavian artery.

In a number of animals, femoral artery or abdominal aortic pressure was monitored during thoracic aortic occlusion. Upon application of a clamp across the aorta immediately below the left subclavian artery, the abdominal aortic pressure immediately fell to a level of from 40 to 50 mm. Hg. Application of a second clamp to the distal thoracic aorta just above the diaphragm was associated with a further pressure drop to a level of approximately 10 mm. Hg. This variation was also studied in relationship to time (Fig. 7). It was found that over a period of 80 minutes the blood pressure in the abdominal

aorta was consistently higher in an animal with one clamp occluding the upper descending aorta than in an animal with proximal and distal occlusion of the descending thoracic aorta. In 6 animals, inferior vena caval blood flow was measured during thoracic aortic cross-clamping (Fig. 8). The flow of

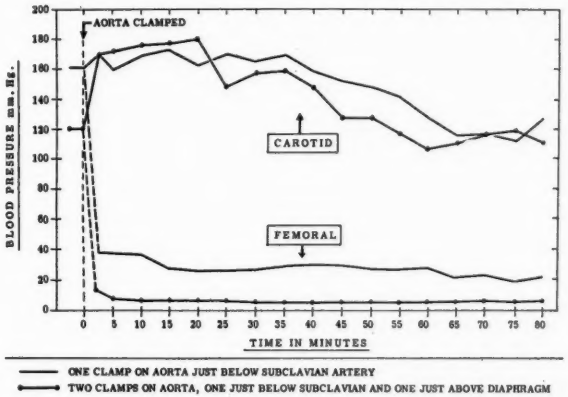
AORTA CLAMPED
CAROTID
FEMORAL
BLOOD PRESSURE mm. Hg.
TIME IN MINUTES
ONE CLAMP ON AORTA JUST BELOW SUBCLAVIAN ARTERY
TWO CLAMPS ON AORTA, ONE JUST BELOW SUBCLAVIAN AND ONE JUST ABOVE DIAPHRAGM

Fig. 7.—Graph showing mean carotid and femoral blood pressures in 2 dogs during an 80-minute period of time. In one, the aorta was occluded with one clamp placed just below the base of the subclavian artery. In the other, the descending aorta was doubly cross-clamped, one clamp located below the base of the subclavian and the other just above the diaphragm.

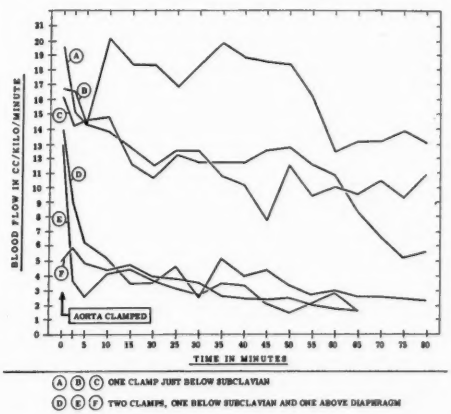
BLOOD FLOW IN CC/KILO/MINUTE
AORTA CLAMPED
TIME IN MINUTES
A B C ONE CLAMP JUST BELOW SUBCLAVIAN
D E F TWO CLAMPS, ONE BELOW SUBCLAVIAN AND ONE ABOVE DIAPHRAGM

Fig. 8.—Graph showing rate of blood flow from inferior vena cava in 6 dogs over an 80-minute period of time. In 3 dogs, the aorta was occluded with one clamp placed just below the base of the subclavian artery. In the others, the descending aorta was doubly cross-clamped, below the base of the subclavian and just above the diaphragm.

blood through the inferior vena cava was consistently quite low when the aorta was clamped just beyond the left subclavian and just above the diaphragm and was approximately four times greater in those animals in which a single occluding clamp just beyond the subclavian was used.

CLINICAL OBSERVATIONS

Superior vena caval-femoral by-pass was used in 4 clinical cases and brachial-femoral by-pass in one. Heparin was administered at the time of insertion of the catheters and the patient was fully heparinized during the by-pass procedure. Afterward protamine was given. The cannulated internal jugular veins were ligated. When the profunda femoral artery was cannulated, it was subsequently ligated, and when brachial and common femoral arteries were utilized, the arteriotomies were closed with 5-0 silk sutures.

CASE 1.—The patient was a 66-year-old white woman who was admitted with a diagnosis of thoracic aortic aneurysm. On June 12, 1956, she was taken to the operating room and a large plastic catheter was introduced through the internal jugular vein into the superior vena cava and through the right profunda femoral into the iliac artery. The upper lobe of the lung was densely adherent over a large aneurysm, about 12 cm. in diameter, arising immediately distal to the origin of the left carotid artery. After isolating the aorta proximally and distally, a by-pass shunt of 20 c.c. per kilogram per minute was instituted. The rate of flow was 1,000 c.c. per minute. The arch and the descending aorta were cross-clamped. In applying the proximal clamp, the diseased left common carotid was disrupted near its point of origin necessitating clamping the arch proximal to the left common carotid origin as well as the carotid itself. The aneurysm was removed and a nylon graft interpolated. The carotid was then re-approximated. The clamps were in place 70 minutes. A good recovery was made and at present the patient is leading an essentially normal life.

CASE 2.—The patient was a 32-year-old man admitted for the third time. During his first admission, in 1946, he was found to have a patent ductus arteriosis complicated by bacterial endocarditis. The ductus was ligated but it subsequently recannulized. In 1950, exploration revealed such a large ductus and aneurysm that the procedure was abandoned. He developed episodes of congestive failure and by 1956 was thought to be reaching the terminal stage of his disease unless the underlying abnormality could be corrected. On June 18, 1956, plastic catheters were passed from the internal jugular vein into the superior vena cava and from the right profunda femoral artery into the iliac. A large calcified aneurysm of the ductus and pulmonary artery was found. After isolating the pulmonary artery and aorta and clamping them proximally and distally, the ductus was divided. Immediately beforehand a by-pass from superior vena cava to femoral artery was begun at the rate of 20 c.c. per kilogram per minute. The 6 cm. long defect in the aorta was repaired, and the clamps released and the pump stopped. The clamps were on for 30 minutes. In resecting the aneurysm, which was densely adherent to the arch, a tear occurred underneath the base of the arch necessitating arch and aortic clamping for an additional 10 minutes for suture closure of the rent. The by-pass was used during this 10-minute period. After excising the aneurysm, the defect in the pulmonary artery was closed by suture. The patient made a good recovery and has remained well.

CASE 3.—The patient was a 63-year-old white man who was admitted with a large thoracic aneurysm and positive serologic tests for syphilis. On Oct. 3, 1956, plastic catheters were inserted into the superior vena cava and femoral artery. A large aneurysm beginning at the base of the heart and extending down to the diaphragm was found. The most prominent part of the aneurysm, however, was from the base of the left subclavian to the diaphragm. The proximal aortic clamp was placed proximal to the origin of the subclavian and the distal clamp just above the diaphragm. Beforehand the by-pass was begun at a rate of 20 c.c. per kilogram per minute. The shunted blood was dark in color. The aneurysm was excised and a nylon filter fabric graft was interpolated. The clamps were removed 60 minutes after application. The aneurysm was densely adherent to the mediastinum and bulged into the right thorax, necessitating excision of the mediastinal pleura. The left

thorax was dry at the completion of the procedure, but following operation the patient continued to lose blood through the left chest tube. Even though this was replaced, he remained hypotensive. He was conscious and moved both lower extremities well. It was decided that exploration for bleeding points should be carried out, but before it could be done he died suddenly. Autopsy revealed the right chest to be filled with blood, apparently from transsection of pleural vessels in the right hemithorax.

CASE 4.—The patient was a 76-year-old white man with an aneurysm of the descending thoracic aorta. On Dec. 3, 1956, plastic catheters were inserted through the profunda femoral into the common femoral artery through the internal jugular vein into the superior vena cava. The lung was adherent everywhere to the chest wall and aneurysm. The aneurysm was found to arise 3 or 4 cm. below the subclavian and to extend down to just above the diaphragm. The mechanical by-pass was started at a rate of 20 c.c. per kilogram per minute and the aorta was clamped above and below the aneurysm. The shunted blood was dark in color. The aneurysm was resected and a nylon filter fabric graft interpolated. The aorta was cross-clamped 70 minutes. The right leg in which the plastic catheter had been inserted was found to be completely ischemic. Blood flow could not be restored even after opening the common femoral artery and doing a thromboendarterectomy of the common and superficial femoral arteries. A by-pass graft was then sutured end-to-side into incisions in

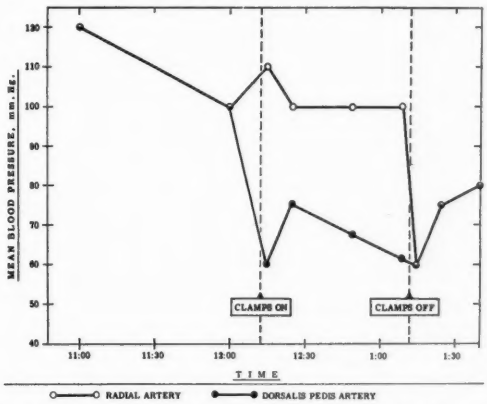

Fig. 9.—Graph of mean radial and dorsalis pedal arterial blood pressures in Case 5 (W. K.) before, during, and after the descending aorta was cross-clamped. A brachial to femoral artery by-pass at a rate of 15 c.c./Kg./min. was functioning during the period of aortic occlusion.

the popliteal and femoral arteries. Adequate circulation was then present in the extremity. The patient seemed to be regaining consciousness and moved both lower extremities. He remained hypotensive, however, and bloody fluid drained from the chest tube. The thorax was re-opened and was found to be filled with blood. Diffuse bleeding from the lung and the surfaces of the pleura and diaphragm was noted. The patient had received considerable blood beforehand and the character of the bleeding suggested a hemolytic reaction. After applying hot packs and using the cautery and ligatures, it appeared as though hemostasis had been obtained. Following this second procedure the patient did poorly. There was drainage of bloody fluid from nose, oral cavity, and rectum. He did not entirely regain consciousness and in a few hours died.

CASE 5.—The patient was a 30-year-old white man who was in an automobile accident in 1947 and had been subjected to an exploratory thoracotomy elsewhere in 1957. A thoracic aneurysm was discovered on that occasion. He was operated upon on March 22. Plastic catheters were inserted into the right brachial and left common femoral arteries. The

aneurysm arose at the level of the ligamentum arteriosum and extended distally a distance of about 4½ inches. The aorta was clamped and the aneurysm excised. A nylon graft was interpolated. The aortic clamps were released one hour after their application during which time a by-pass shunt of 15 c.c. per kilogram per minute had been maintained. Before, during, and after the procedure, radial and dorsal pedal pulses were monitored and renal blood flow studies were carried out. During the time of aortic clamping, radial artery pressure did not rise appreciably and dorsal pedal pressure ranged between 60 and 75 mm. Hg (Fig. 9). Blood pressure returned to normal levels shortly after the operation was completed. Renal function as measured by inulin and para-aminohippuric acid excretion fell to almost zero levels during the time of aortic clamping. Immediately upon release of the clamps, however, urinary excretion returned and renal plasma flow and glomerular filtration rate returned rapidly toward normal (Fig. 10). There was no period of oliguria during his postoperative convalescence which was uneventful. He had excellent circulation in the extremities in which the cannulas had been inserted.*

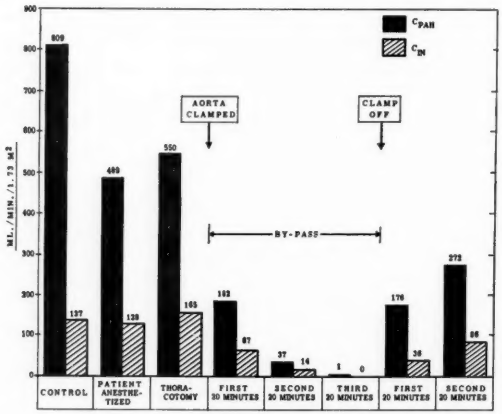

Fig. 10.—Graph showing renal function during operation in Case 5 as measured by para-aminohippuric acid and inulin excretion.

DISCUSSION

Control observations confirmed the general impression that thoracic aortic cross-clamping is extremely hazardous. Pontius and associates[4] reported that when 18 dogs' aortas were clamped below the subclavian artery and just above the diaphragm for an hour, 8 died, 9 survived with paraplegia, and only one lived without paraplegia. Of our 17 animals only one survived without paraplegia, 2 with paraplegia, and the remainder died.

Pontius and his colleagues found the mortality rate was less when a single clamp was placed across the thoracic aorta at the level of the ligamentum arteriosum. Of 11 animals so treated, there was only one death, while 3 survived with paraplegia and 7 without paraplegia. Our observations on blood pressure in the abdominal aorta and on return blood flow through the inferior vena cava furnish a logical explanation of the difference in mortality noted

*The authors wish to acknowledge their indebtedness to Dr. Walter Judson who did the renal function studies in Case 5.

when a single clamp is placed across the upper descending thoracic aorta on the one hand, and when two clamps are placed at the beginning and distal end of the descending thoracic aorta on the other hand. It was found that the abdominal aortic blood pressure was maintained at a level approximately four times greater when only a single clamp was used. Similarly, measured blood flow through the inferior vena cava demonstrated that it was approximately four times greater in those animals in which the aorta was clamped at a single level rather than at the first and distal portions of the descending thoracic aorta. These observations, obviously have some clinical significance. It has certainly been demonstrated in patients that exclusion of blood flow through a relatively short segment of the thoracic aorta is better withstood than exclusion of a long segment such as is usually necessary in the excisional treatment of large aneurysms.

When these experiments were initiated, the first preliminary observations were made with a measured by-pass from left atrium into the femoral artery. Observations made during these preliminary studies indicated that, when the thoracic aorta is occluded, the superior vena caval blood becomes more fully saturated with oxygen. That such should be the case seems logical in view of the marked increase in flow of blood through the superior vena cava during aortic occlusion. Since there are clinical situations in which it is necessary to occlude the thoracic aorta and in which it is technically rather inconvenient to isolate and cannulate the left atrium, it seemed desirable to study the feasibility of withdrawing blood from a more convenient site. In view of the fact that the superior vena caval blood seemed regularly to be very well saturated with oxygen, the superior vena caval-femoral by-pass appeared logical. It also seemed likely that the hypoxic tissues in the lower portion of the body would extract oxygen even from blood which was not fully saturated. Experiments with shunting blood from the superior vena cava to the femoral artery in varying moderate amounts did indeed demonstrate excellent protection. Only one of 24 animals so treated died after an hour's cross-clamping of the thoracic aorta and there were no instances of paraplegia.

This method was used in 4 clinical cases. In 2 of them the by-pass went well, the blood picked up from the superior vena cava was grossly well saturated, and the patients recovered uneventfully. In 2 patients it was noted, however, that the blood coming from the superior vena cava was not well saturated. Both of these patients died. They recovered, however, sufficiently so that it was clear that they had no neurologic damage. In both cases the cause of death was obviously hemorrhage. In one it was clearly the result of a transfusion reaction and in the other it was apparent that pleural vessels on the right side of the mediastinum were transsected and continued to bleed.

Because of the occasional animal in which the expected high oxygen saturation of the superior vena caval blood was not observed, and because in 2 patients the blood picked up from the superior vena cava was grossly not well oxygenated, it was decided to test the feasibility of a similar by-pass from

brachial to femoral artery. The experimental results were altogether gratifying. There were no instances of paraplegia. A single dog which at post-mortem examination had a sizable hemothorax died. The one clinical experience was good.

Our observations have been limited to relatively low flows into the trunk and lower extremities. It is well established that reduced flows of blood can be used successfully during temporary cardiopulmonary by-pass.[18, 19] Our data would indicate that the low flow technique can also be used in by-passing the occluded thoracic aorta. These small shunts of blood protect the experimental animal well for at least an hour and the same seems to be true with regard to patients. Such low flow by-pass shunting has eliminated paraplegia in the experimental animals and none of the patients exhibited weakness of the extremities. Furthermore, there was no postoperative evidence of impairment of urinary output either in the experimental animals or the patients. In the one patient in whom renal blood flow studies were carried out during the procedure there was a prompt resumption of renal blood flow immediately upon release of the aortic clamps and the patient had no period of oliguria, postoperatively. We do not know whether somewhat larger flow rates would be desirable nor have we determined the maximum or minimum flow which is possible using the brachial artery as the source of blood.

The use of a low flow by-pass appears to be definitely a better protective procedure than hypothermia. Pontius and his associates found that general hypothermia eliminated paraplegia in surviving animals but did not lower the mortality. This observation was confirmed by Parkins and his associates.[6] Clinically we have the same impression. In using hypothermia for cases in which the thoracic aorta had to be cross-clamped, we encountered a number of difficulties which seemed directly attributable to hypothermia including the occurrence of fatal ventricular fibrillation.

Of the two methods studied it is our feeling that artery-to-artery by-pass is altogether preferable. This method has two, at least, theoretic disadvantages. One concerns the necessary use of anticoagulants. Extensive employment of anticoagulants during operative procedures, particularly with cardiopulmonary by-pass, would indicate, however, that ordinarily this theoretic objection to heparin is not of great practical significance. The other concerns possible obstruction of the cannulated artery. In one patient with rather marked disease at the bifurcation of the common femoral artery, the catheter was introduced through the profunda femoral. When the thoracic operation was completed it was clear that the patient had femoral artery obstruction undoubtedly due to dislodgment of a plaque by passage of the catheter and in this case it was necessary to do a by-pass graft. It is our impression, however, that if the operator selects a peripheral artery into which the catheter can be passed without trauma, the chances of ischemic consequences are relatively small. These possible objections are more than outweighed by certain advantages. No reservoir of blood is required and the necessity for constantly watching a blood level is eliminated. The use of the brachial and femoral arteries removes the shunt

from the field of operation and allows the operator to confine his attention to the operative procedure itself. The aortic excision is not restricted to the descending aorta as is true in certain other types of temporary aortic by-pass shunts. The distal arch can be occluded if necessary. The pick-up and out-flow cannulas are easily and quickly inserted and removed. The repair of the small arteriotomies is accomplished more quickly and easily than suture closure of the aorta when temporary graft by-passes are employed. With the mechanical by-pass one can be certain at all times that the shunt is functioning and at a known rate of flow. Body temperature is not significantly lowered during the operation and risk of ventricular fibrillation from quickly induced hypothermia should be very small.

CONCLUSIONS

Experiments are presented which demonstrate that either a small measured mechanical by-pass from the superior vena cava to the femoral artery or from the brachial to the femoral artery eliminates almost entirely the hazard of the dire consequences of prolonged thoracic aortic cross-clamping. Experimental observations indicate that, while the thoracic aorta is cross-clamped, the flow of blood returning to the superior vena cava is increased and its oxygen saturation generally augmented almost to levels of arterial blood. Such by-pass shunts increase the blood pressure in the distal arterial segments. The observed differences in risk with exclusion of a small segment of the thoracic aorta, on the one hand, and a long segment, on the other, would seem explainable on the observed differences in distal arterial pressure and in inferior vena caval flow under the two circumstances. The use of either type of by-pass in patients appears to be feasible and adds safety to operative procedures requiring clamping of the thoracic aorta. Of the two methods, brachial artery to femoral artery by-pass seems the preferable.

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DISCUSSION

DR. M. E. DEBAKEY, Houston, Texas.—I should like to express appreciation for these valuable observations of Dr. King and Dr. Shumacker in their method of providing by-pass circulation during cross-clamping of the aorta. We have been particularly interested in this method of control by extracorporeal circulation. Our interest developed a little over a year ago when we, like others, were searching for better methods of overcoming the potential ischemic changes that might occur from temporary occlusion of the aorta. We have, of course, previously used hypothermia, and recognized both its advantages and disadvantages. But in light of the need for some better method it seemed to us that this might be accomplished by controlled extracorporeal circulation. However, our efforts were directed toward the use of arterial blood rather than blood from the venous system. From our past experience with the problem of resection of aortic aneurysms requiring occlusion of the aorta, and from our laboratory experience with dogs, we are convinced that there are certain factors that operate in human beings that differ from those that operate in dogs. It has become apparent to us that patients with aneurysms can tolerate a longer period of aortic occlusion than can the normal dog. It has been fully demonstrated so far as we are concerned that in most cases of aneurysms located in the distal part of the descending thoracic aorta it is unnecessary to employ hypothermia, by-pass, or other means of combating the ischemic effects of temporary occlusion of the aorta. In such cases temporary arrest of aortic circulation for the period required to excise and repair the defect, usually less than 45 minutes, is well tolerated.

However, in cases in which the aneurysm is located more proximally, it does become necessary to employ some method of overcoming the potential ischemic effects of circulatory arrest. For this purpose we have employed two methods of controlled extracorporeal circulation. (slide) One of the methods is illustrated in this drawing showing its use for resection of aneurysms located distal to the left common carotid artery. By means of a catheter inserted in the left auricle, arterial blood is derived from this source and perfused into the distal aorta by means of a pump connected with a catheter inserted through the left femoral artery. The pump permits regulation of the flow rate as well as the blood pressure, thus assuring control of both of these factors.

(slide) The other method is employed in cases in which the aneurysm is located in the proximal portion of the aortic arch as illustrated in this slide. Under these circumstances it becomes necessary to do cardiopulmonary by-pass and therefore to use the artificial heart-lung apparatus. In this case, for example, the fusiform aneurysm involved the ascending aorta and transverse arch, necessitating application of occluding clamps to the base of the ascending aorta, the innominate, left common carotid, and left subclavian arteries and to

the descending aorta. Using the artificial heart-lung apparatus, total cardiopulmonary by-pass was done perfusing oxygenated blood into the distal aorta as well as both common carotid arteries for a period of 45 minutes during which time the aortic arch was resected and replaced with an aortic homograft.

(slide) This is a photograph taken at operation after completion of the homograft replacement. One may observe the proximal anastomosis lying at the aortic outlet from the heart, the anastomosis to the innominate artery, to the left common carotid artery and to the distal aorta at the base of the left subclavian artery. This patient had an uneventful postoperative course and follow-up examination approximately 2 months after operation revealed normal findings and resumption of normal activities.

DR. SANFORD E. LEEDS, San Francisco, Calif.—About four years ago, before the American College of Surgeons, we reported a small group of animal experiments in which blood was drawn by cannula from the left carotid artery and passed to a reservoir, then to a pump and into a plastic catheter passed up a femoral artery to a point just below the cross-clamped aorta; very similar to what Dr. King has reported. The only point we might add to this excellent presentation is that some of our animals were cross-clamped for a period of 3 hours, and none of these animals showed any ischemic damage to the spinal cord or any other deleterious effects. If the blood entered the femoral artery by cannula, or the plastic tubing was not passed into the thoracic aorta to the cross-clamped area, the protection of the spinal cord was not so effective.

DR. FRANK GERBODE, San Francisco, Calif.—I want to compliment Drs. King and Shumacker on their very excellent paper and to report some laboratory and clinical experiences with a similar approach to preservation of the spinal cord and visceral function during cross-clamping the aorta. Dr. Braimbridge has been associated with me in the laboratory in experiments along these lines. In the dog, we found that by connecting a plastic catheter with an inside diameter of 2 mm. between the femoral arteries we got enough flow to protect the dog against 1½ hours of aortic occlusion without death and without paralysis. These experiments were done without the aid of a pump. This means, therefore, that a very small flow, as Dr. Shumacker has pointed out, is required to keep the cord alive and even to supply the viscera with sufficient blood. In other experiments we employed a similar technique, as recently described by Dr. DeBakey, of using a shunt between the left atrium and the femoral artery. This also protected the cord and visceral function. It requires a pump and heparinization. This technique has distinct advantages found also in our clinical application in 5 cases of thoracic aneurysm. It is necessary to monitor the blood pressure in the proximal and distal arterial systems, for extreme fluctuations may occur which require adjustments in the pumping rate. At present we monitor the proximal pressure through the right radial artery.

ELECTIVE CARDIAC ARREST—AN ADJUNCT TO OPEN-HEART SURGERY

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CLEVELAND, OHIO

THE initial report by Melrose and associates[1] on laboratory observations of elective cardiac arrest was published in July, 1955. This team of English workers recognized the importance of a dry motionless field in the development of open-heart surgery. Their approach, based on the early work reported by Ringer,[2] in 1883, and Hooker,[3] in 1929, was further stimulated by the more recent publications of Montgomery, Prevedel, and Swan.[4] Melrose and co-workers[1] developed a simple technique using a potassium citrate–blood mixture for inducing elective cardiac arrest in dogs. Although they did not report clinical application, their concept of elective cardiac arrest and the simplicity of their method had particular appeal to us. The decision to employ this technique at the Cleveland Clinic was made after an intensive experimental trial.

EXPERIENCE

On Feb. 17, 1956, the Melrose technique of elective cardiac arrest was utilized in the closure of an interventricular septal defect.[5] The patient, a 17-month-old child, is thought to be the first clinical case in which elective cardiac arrest was successfully employed.

Since the initial operation, elective cardiac arrest has been utilized by the authors in 73 operations; a total of 84 open cardiotomy procedures have been performed with the aid of pump-oxygenators. Cardiac arrest has been employed in operations for closure of septal defects at the auricular and ventricular levels, correction of mitral and tricuspid insufficiency, aortic valvular commissurotomy, correction of pulmonic valvular and infundibular stenosis, and in attempts to correct transpositions of the great vessels. On the basis of this experience, a preliminary conclusion is justified, namely: the safety and the benefits provided by the Melrose technique for elective cardiac arrest justify its use in surgery on the open heart.

From the Departments of Thoracic Surgery and of Cardiovascular Disease, and the Division of Research, The Cleveland Clinic Foundation and The Frank E. Bunts Educational Institute, Cleveland, Ohio.

Read at the Thirty-seventh Annual Meeting of The American Association for Thoracic Surgery at Chicago, Ill., May 4-7, 1957.

ADVANTAGES

The ideal surgical field is one that provides freedom from motion, good exposure, and reasonable hemostasis; each of these criteria is fulfilled by elective asystole. Complete cessation of motion to permit unhurried and careful inspection of a cardiac abnormality is in itself invaluable to the surgeon; it is obvious that a more precise operation is possible than when the heart is beating. Moreover, conservation of blood is abetted, as the coronary circulation ceases during the open cardiotomy.

Another less apparent advantage of elective cardiac arrest is that the flaccid heart may be raised from its pericardial bed so that it can be displaced or manipulated to expose every aspect. When the heart is in asystole each of the four major chambers is directly accessible and each may be entered as the indications direct. Reluctance to enter the left side of the heart based on fear of fatal air embolus is needless when the heart is stopped.

Heart block seems to be less common when cardiac arrest is employed than when it is not used. The possible explanation for this fact deserves further study. It may be that serious heart block is not the result of mechanical suture occlusion of conduction fibers. It is possible that local myocardial ischemia and the resultant anoxia may exert far greater influence than does the trauma of an encircling suture. Local ischemia, particularly in the ventricular septum, may occur when the sutures tear or occlude portions of the muscular septum during operations on the beating heart. In any event, cardiac block apparently is less common in operations where a high perfusion rate has been maintained and the heart has been arrested during the intracardiac procedure.

TECHNIQUE

The basic concept of stopping and restarting a human heart may sound as though it would be complicated to achieve; actually it is simple. Although other methods have been reported in which combinations of drugs are used, with or without hypothermia, the Melrose technique utilizes only one drug, and for equipment requires only a syringe, an injection needle, and an occluding clamp. The simplicity and the effectiveness of the method have added to the value of this adjunct to intracardiac surgery.

Stopping the Heart.—The heart is prepared in the conventional manner for circulation bypass through the pump-oxygenator. It is our practice to cannulate both venae cavae through separate stab wounds in the posterior aspect of the right auricle. The arterial flow from the pump-oxygenator is returned via a subclavian or common femoral artery. The aorta is then isolated by sharp dissection and an umbilical tape is placed around it. The point of isolation usually is made from 2 to 3 cm. distal to the coronary ostia; this is the only additional dissection that is required for elective cardiac arrest. After the patient is on the pump-oxygenator "run" and the perfusion has been stabilized, the caval tourniquets are tightened to complete the venous bypass. Within 2 minutes, the right side of the heart is seen to decompress partially and the aorta to soften as the output of blood is reduced. An occluding clamp

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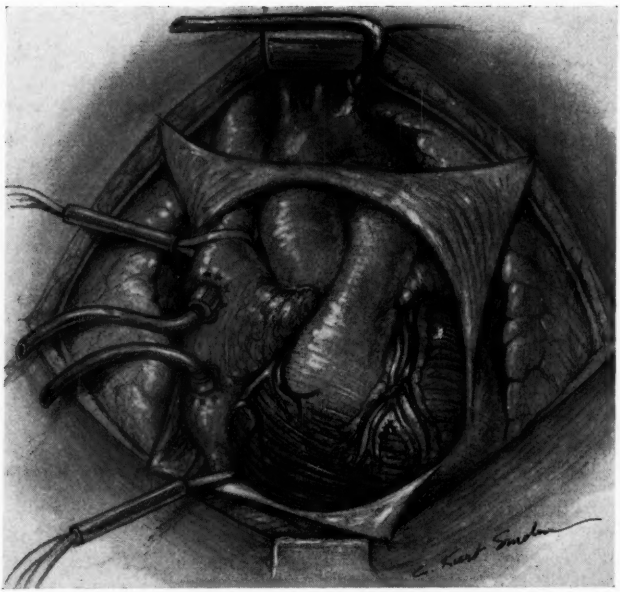

Fig. 1.—This drawing depicts the usual cannulation for bypass of the heart and lungs. The cannulae in the right auricle pass into each vena cava. Blood may be returned either into the left subclavian artery as shown here or into one of the femoral arteries in the groin.

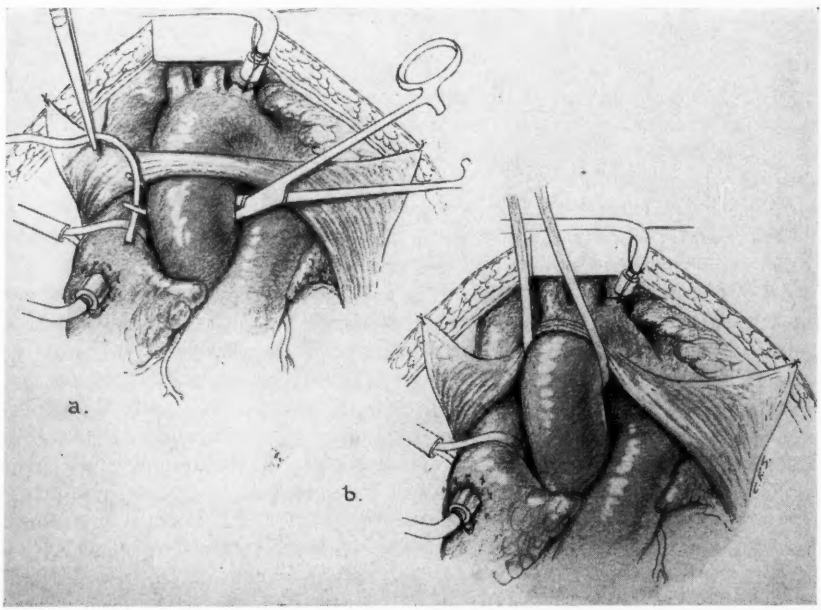

Fig. 2.—Mobilization of the aortic arch as shown here is the only additional dissection necessary for application of elective arrest with potassium citrate.

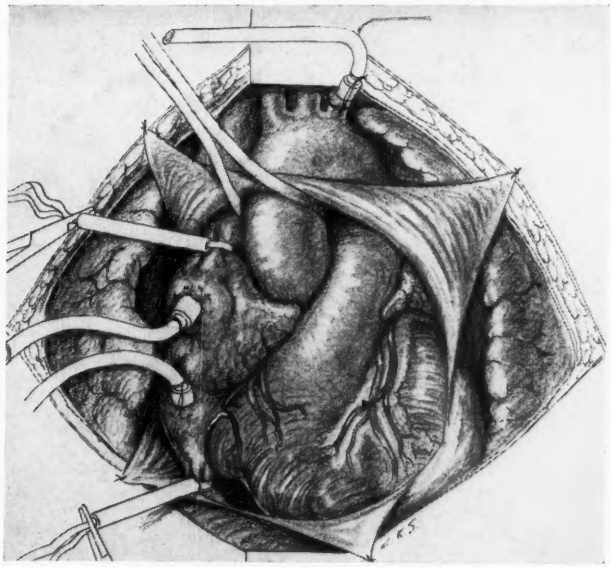

Fig. 3.—When the occluding ligatures about the venae cavae are snugged down and all of the venous return is diverted to the pump-oxygenator, the exposed right side of the heart quite rapidly becomes relatively empty and soft. Similarly the aortic pressure will fall to the level that can be maintained by the pump-oxygenator flow.

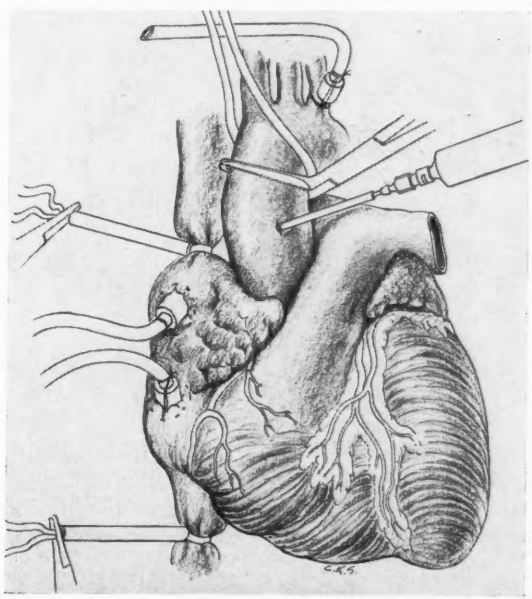

Fig. 4.—When a few beats have maximally emptied the heart of blood, a noncrushing clamp is placed across the previously mobilized aorta and the potassium citrate solution is injected proximal to the clamp; thus the injected solution must enter either the coronary arteries or the left ventricle, should the aortic valve be incompetent. Note the small segment of plastic catheter placed over the needle to control the depth of penetration into the aorta.

then is placed across the aorta at the previously selected site. A variety of clamps are available for this purpose; the Potts ductus or the Potts coarctation clamp is used most frequently. Injection of the potassium citrate–blood mixture* is then made directly into the proximal aorta and is continued until the heart is stopped. In children the amount of the blood mixture required to induce cardiac arrest may vary from 6 to 20 c.c.; adults with cardiomegaly may require as much as from 150 to 200 c.c. The dose, however, is that amount of the potassium citrate mixture that will induce complete cardiac arrest. Within reasonable limits there does not appear to be any such thing as overdose or unwarranted side effects from the drug itself.

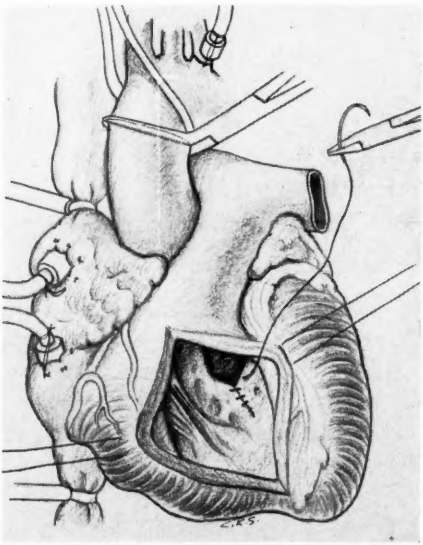

Fig. 5.—The potassium-arrested heart is remarkably flaccid and in most instances defects may be closed side-to-side without tension. In the absence of significant collateral circulation to the lungs, once the heart is emptied of blood at the time of the initial incision, it remains remarkably dry. In the presence of extensive collateral circulation, of course, this will return to the left side of the heart via the pulmonary veins and also to the right side of the heart via the pulmonary artery.

The heart appears to dilate as its motion ceases and there is complete relaxation of all muscle fibers. It must be remembered that blood is still able to enter the heart through the bronchial vessels and any collateral circulation that may exist between the aorta and the lungs. This blood flow will appear to be arterial, as it is coming directly from the pump-oxygenator via the bronchial or collateral pathway; it is negligible and easily controlled by the surgical aspirator, except in severe cases of cyanotic heart disease. If a

*The potassium citrate–blood mixture is standard for all operations and is freshly prepared by the surgical nurse. Two cubic centimeters of a 25 per cent solution of potassium citrate is added to 18 c.c. of heparinized blood taken from the oxygenator reservoir. Several 20-c.c. syringes with this mixture may be prepared if larger doses are anticipated. Accurate, rapid injection is easier with the 20-c.c. syringe than one containing a larger volume.

patent ductus is present there will be a large retrograde flow from the pulmonary artery. This flow, of course, is handled by prompt diagnosis and occlusion of the ductus. When the heart is opened the blood therein may be removed through a sterile suction apparatus for re-use if desired. As stated before, the flaccid heart may be manipulated as necessary without fear of creating conduction problems. Since time no longer is the important factor, the surgeon may perform the intracardiac operation with calm deliberation.

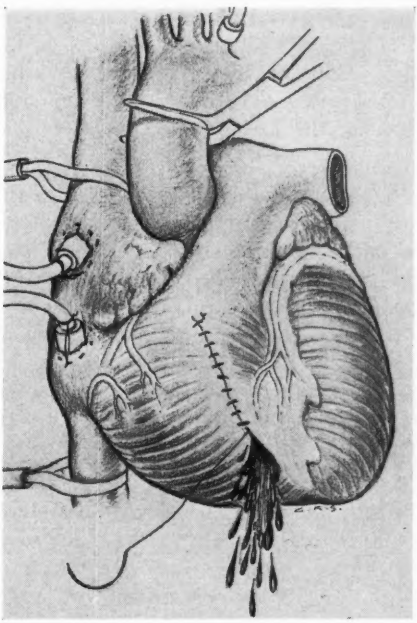

Fig. 6.—The heart is restarted by restoring coronary perfusion, by removing the occluding aortic clamp. Ordinarily the occluding caval tapes are removed at the same time. If convenient, a portion of the cardiotomy incision may be left open a few moments after removal of aortic occlusion. In this way the first high-potassium coronary return may be partially flushed out of the circulation.

Restarting the Heart.—When the operation has been completed and the cardiac incision has been closed, the heart is restarted by re-establishing coronary perfusion. It is our practice to release the caval tourniquets first and then to remove the occluding clamp from the aorta. The perfusion from the distal aorta returns to the coronary system and within a matter of seconds the potassium solution is flushed into the coronary sinus where it enters the general circulation. It was our early practice to release blood from the partially closed ventriculotomy incision in an effort to remove most of the potassium. It appears now that this procedure is unnecessary, because of the great dilution from the patient's circulation and that of the extracorporeal mechanism. A high flow rate of perfusion is the most effective means of restoring a good heartbeat. Within 2 minutes the auricle should begin active

contraction and shortly thereafter the first ventricular systoles will be seen. It should be emphasized that no additional drugs are necessary and the routine use of calcium or atropine is to be avoided. The heartbeat becomes progressively more forceful and the myocardium shows steady improvement in color due to improved oxygenation. It is our practice to continue the high flow rate of perfusion for a period of from 4 to 6 minutes, and if the heartbeat is effective, the pump-oxygenator "run" is discontinued for a trial period. If the heart maintains an adequate arterial pressure, and the tracings on the electrocardiograph and the electroencephalogram are satisfactory, the operation is terminated. If the arterial pressure drops or the electroencephalogram shows depression of the brain waves, it is advisable to return the patient's circulation to the pump-oxygenator until the difficulty is corrected. These periods of "second runs" are less frequent after the team has acquired experience.

RESULTS

As stated before, complete asystole has been employed in 73 operations for a wide variety of cardiac abnormalities. In 2 patients the heart was not resuscitated; both patients were operated upon for aortic stenosis and in each case the right coronary artery was mechanically occluded through technical error. As would be expected, the returning heartbeat repeatedly degenerated into ventricular fibrillation. Early in our experience, the operation on an infant with cor triloculare was unsuccessful. Although the heartbeat re-

TABLE I. DIAGNOSIS WITH RESULTS IN 84 INTRACARDIAC OPERATIONS*

DIAGNOSIS	NUMBER OF PATIENTS	WITH CARDIAC ARREST (NO. OF PATIENTS)		WITHOUT CARDIAC ARREST (NO. OF PATIENTS)	
		SURVIVED	DIED	SURVIVED	DIED
1. Interventricular septal defect	30	21	8	–	1
2. Interventricular septal defect with mitral stenosis	1	1	–	–	–
3. Cor triloculare (bi-atrium)	2	–	2	–	–
4. Interatrial septal defect	7	1	1	4	1
5. Interatrial septal defect with mitral insufficiency	2	1	1	–	–
6. Interatrial septal defect with mitral stenosis (Lutembacher's syndrome)	2	–	2	–	–
7. Interatrial septal defect with pulmonic stenosis	1	1	–	–	–
8. Ostium primum with mitral insufficiency	2	1	1	–	–
9. Mitral insufficiency	3	2	1	–	–
10. Pulmonic stenosis					
Valvular	6	1	–	5	–
Infundibular	1	1	–	–	–
11. Aortic stenosis					
Congenital	3	2	1	–	–
Acquired	3	1	2	–	–
12. Tetralogy of Fallot	16	9	7	–	–
13. Transposition of great vessels	3	–	3	–	–
14. Corrected transposition	1	–	1	–	–
15. Primary pulmonary hypertension	1	–	1	–	–
Total	84	42	31	9	2

*Data through April 15, 1957.

turned, the output was inadequate and the patient died within an hour after leaving the operating room. In the other patients, including those who ultimately died after surgery, a satisfactory heartbeat was re-established.

DISCUSSION

When the arrested heart is reperfused by oxygenated blood, a satisfactory rhythm should resume spontaneously. If this does not occur or a serious arrhythmia develops, the causative factor must be recognized. The reasons for failure are related invariably to myocardial anoxia. If the cause is recognized and corrected, the cardiac response usually is gratifying. Analysis of our own difficulties, particularly in the early cases, reveals four major causes for myocardial anoxia: (1) inadequate blood flow from the pump-oxygenator, (2) faulty cannulation of the arterial line, (3) coronary air emboli, (4) mechanical occlusion of a major coronary vessel.

Recognition of these four difficulties has been of inestimable value to us and has led to revision of our technique. Higher blood flow rates are now being used in all patients, particularly in children. With larger flow the heart starts more quickly and with greater vigor; at the same time lessening the problem of metabolic acidosis. Better methods of cannulation, especially in the presence of degenerative vascular disease, have been conducive to better myocardial perfusion and a lower incidence of troublesome arrhythmias. The matter of coronary air emboli deserves particular consideration. Operations involving the left side of the heart permit air bubbles to be trapped in the interstices of the left ventricle. As the heartbeat resumes, this air will be extruded into the proximal aorta where it will be diverted by the perfusion flow into the coronary vessels. The presence of air emboli in the coronaries will be attendant with local myocardial ischemia, and this frequently initiates ventricular tachycardia or fibrillation. It is not difficult to recognize the air bubbles; the treatment is basically simple. An increase in the coronary perfusion will drive the air through the vessels into the venous return, where it becomes lost in the circulation of the right side of the heart. When this has been accomplished, it is not unusual for the ventricular arrhythmia spontaneously to revert to an effective sinus rhythm. Ventricular arrhythmia that occurs in the patient who is supported by the pump-oxygenator is of little consequence if eventual conversion is obtained. While satisfactory extracorporeal circulation is maintained, the time factor is of relatively little importance and, at this stage, patience on the part of the surgeon is indeed a virtue. If ventricular fibrillation persists after the obvious cause has been corrected, the surgeon may then elect to defibrillate the heart by electric shock.

The time limit of elective cardiac arrest has not been determined. In the laboratory, the canine heart can be resuscitated after 3 hours of arrest. The dog's heart can be stopped and restarted over and over again for indefinite periods without apparent damage. As a practical approach, in clinical cases we have limited the period of cardiac arrest to the length of time required to accomplish the intracardiac repair. In the 73 operations here, the shortest

period of asystole was 6 minutes, and the longest 58 minutes. Patients have recovered after more than 2 hours of continuous perfusion from the pump-oxygenator when troublesome arrhythmias occurred. It would seem that the length of time that elective cardiac arrest can be tolerated may be measured in hours rather than in minutes. There is no correlation between the length of the period of asystole and the time required to establish an effective heartbeat.

It would be misleading to state that our faith in elective cardiac arrest has been unwavering from the start. All surgeons have an understandable reluctance to tamper with "the most vital" of all vital functions, the heartbeat. Early experience in the laboratory convinced us that stopping the heart was no problem, but restarting it was, since many of the experimental animals developed ventricular fibrillation after arrest. Although considerable effort was made to improve every technical facet of the procedure, the fact remains that the dog's heart is less cooperative than is its human counterpart.

The venture into open-heart surgery requires team organization and preparatory work in the laboratory. The policy of accepting only seriously ill patients for operation and deferring the better-risk patients has been accompanied by a high mortality. This policy has enforced a rigid, critical attitude toward every phase of the open-heart technique. Many of our early practices relative to extracorporeal perfusion have been modified, the selection of patients has been changed, methods of postoperative care have been improved, and the search for better equipment continues. With the constant flux in methods only one technical adjunct remains firmly entrenched and basically unchanged in our organization and that is the use of elective cardiac arrest for open-heart surgery.

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(For Discussion, see page 518)

EXPERIENCES IN THE USE OF CARDIOPLEGIA (INDUCED CARDIAC ARREST) IN THE REPAIR OF INTERVENTRICULAR SEPTAL DEFECTS

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THE demonstration by Lillehei and his associates at the University of Minnesota that closure of interventricular septal defects by suture under direct vision is feasible has widened the scope of cardiac surgery to a remarkable degree. The first methods of by-passing the heart and lungs by cross circulation with a human donor[1, 2] and by a heterologous lung or reservoir system[3] were soon and happily replaced by a simple and inexpensive mechanical oxygenator of the bubble type.[4] In the meantime, Kirklin and his associates[5] at the Mayo Clinic had used successfully an oxygenator of the Gibbon type for the closure of ventricular septal defects. Although, in the hands of these pioneers, the technical aspects of the operation were excellent as compared with the attempts at obliteration of the defects by closed methods,[6-8] there were several obvious opportunities for improvement. First of all, the field was not completely bloodless, since there was a continuous escape of coronary sinus blood from the right atrium via the tricuspid valve. This could be removed by suction and re-used, but more troublesome was the escape of aortic blood as a result of insufficiency from distortion of the aortic valve which usually lies close to the area of repair. To obtain brief periods of relief from this type of obscuring hemorrhage, Lillehei has used intermittent occlusion of the ascending aorta with a snare.

A second opportunity for refinement in the operation for the closure of interventricular septal defect is in regard to the motion of the heart. Ideally perfect suturing is not possible in the beating heart. These two disadvantages, the presence of blood from the coronary sinus and possibly from the aorta, and the movement of the heart, could be obviated by stopping the heart and clamping the ascending aorta.

At the 1955 Meeting of this Association, in a paper entitled "Induced Cardiac Arrest for Intracardiac Surgical Procedures,"[9] we reported experiments in which the heart was stopped with the injection of potassium chloride solution into the left ventricle. With the brain protected by hypothermia, complicated operations were carried out in the atrial and ventricular chambers. Since we had no pump-oxygenator at the time, we had to depend on manual systole to

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The experimental work was supported by a grant from the Michigan Heart Association.

Read at the Thirty-seventh Annual Meeting of The American Association for Thoracic Surgery at Chicago, Ill., May 4-7, 1957.

expell the potassium salt from the coronary system. The heart almost invariably went through a phase of ventricular fibrillation during recovery but this responded well to the usual countershock. In a series of 20 animals, only one had intractable fibrillation. In November, 1955, we began some tests with acetylcholine as the cardioplegic agent and found that it worked well.[10] We noted that it was preferable to inject the drug into the root of the aorta rather than the ventricle. The injection could conveniently be made through a catheter introduced through the right subclavian branch of the brachiocephalic artery of the dog into the ascending aorta. Snaring of the aorta over the catheter caused all of the injection to enter the coronary arteries. Resuscitation could be obtained without fibrillation by massage alone, but obviously the best method was to perfuse the coronaries with oxygenated blood. This was first done with reservoirs of the blood but later, of course, this method was replaced when we obtained a pump-oxygenator of the bubble type in March, 1956. Seven right ventriculotomies in dogs were carried out, with resuscitation of the heart in all.

In the light of this experience, a syringe of acetylcholine was on the operating table at the time of our first operation for the closure of interventricular septal defect on a 5-month-old child, weighing 11 pounds, with a pulmonary artery mean pressure of 94 cm. of water (April 9, 1956). However, the heart was not stopped before the ventriculotomy. We reasoned that it would be a good plan to make the cardiotomy incision to see how difficult the repair would be, and then stop the heart if necessary. Because of the intracardiac blood present and the motion of the heart, we were unable to visualize the defect, which was well hidden in the tiny heart behind papillary muscles and a tricuspid leaflet. At this point, the heart was stopped with acetylcholine and the defect was eventually exposed and partially closed with a few hurriedly placed sutures. Following the ventriculotomy, and the removal of the aortic clamp, the heart began to beat, but complete atrioventricular block was present and the child died in the recovery room. Since that day, no ventricle has been opened until cardiac arrest has been produced with acetylcholine.

In the meantime, interest in induced cardiac arrest had developed, apparently independently, in at least two other centers. In July, 1955, Melrose[12] of the Postgraduate Medical School of London reported on his experiments with "Elective Cardiac Arrest" using potassium citrate as the cardioplegic agent. This method was used clinically in the closure of interventricular septal defects by Effler and his associates.[13] Moulder and his associates at the University of Chicago used acetylcholine arrest in conjunction with hypothermia in experimental[14] and clinical cases.[15] Young, Sealy, and their associates at Duke University used a mixture of magnesium sulfate and potassium citrate to produce induced cardiac arrest.[16]

SURGICAL PROCEDURES

This report is based on an experience in the closure of ventricular septal defects in 53 children ranging in age from 5 months to 9 years. The thoracotomy and cannulation for the attachment of the pump-oxygenator have been carried out along the lines suggested by Lillehei. The transsternal incision enters the third interspace on both sides. We have found it convenient to divide the deeper

structures in the following order: right intercostal space, right internal mammary vessels, sternum, left internal mammary vessels, and left interspace. The left subclavian artery has invariably been used for the inflow cannula from the pump-oxygenator. Distal occlusion of the vessel has been accomplished by ligating the vertebral artery and continuing subclavian (Fig. 1). This gives a slight funnel effect on the artery for the introduction of the largest possible catheter. The introduction of the catheter is facilitated by the insertion of 3 traction sutures of 5-0 silk. Errors in the cannulation of the venous side are apt to be one of the following: the tendency is to insert the cannula into the superior vena cava too far, and into the inferior vena cava not far enough, or possibly into the hepatic vein.

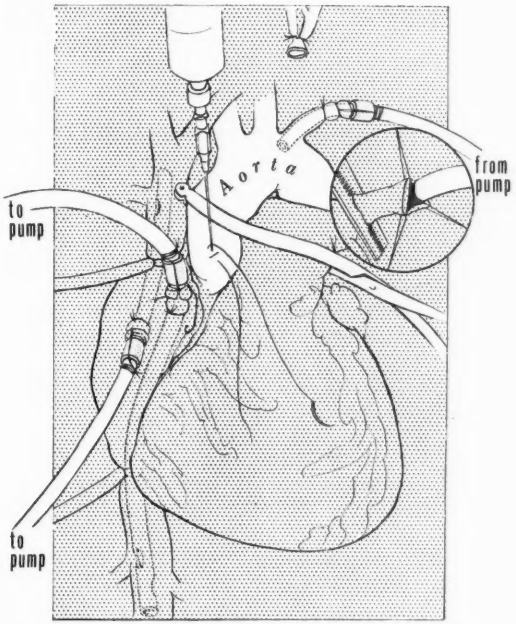


Fig. 1.—Diagram of cannulation of heart for the by-pass with the pump-oxygenator and the method of producing induced cardiac arrest by the injection of the cardioplegic drug into the root of the clamped aorta. *Inset:* Detail of cannulation of the left subclavian artery.

We believe that a definite routine for the maneuvers will establish a habit pattern with the team which may prevent the omission of an essential step in the extracorporeal circulation procedure. The following steps seem to follow each other "geographically": snaring of the venae cavae, testing for patent ductus by compressing the pulmonary artery and feeling for a distal thrill, search for left superior vena cava, mobilization of the subclavian artery, injection of heparin into the right auricle, division and cannulation of the subclavian artery, cannulation of the venae cavae, pump run and cardiotomy, decannulation of venae cavae, decannulation of the subclavian artery, and protamine injection into the right auricle. We have used heparin in the dosage of 1.5 mg.

per kilogram, and have found that it is necessary to use at least twice that amount of protamine to neutralize the heparin remaining after the pump run with heparinized donor blood.

After a minute or 2 of pump run for assurance of free and equal flow of blood in both directions, cardiac arrest is induced in the following manner. For convenience, an umbilical tape sling is passed around the aorta and pulmonary artery. Theoretically, only the aorta need be clamped but separation of the aorta from the pulmonary artery requires some dissection with potential dangers. Also, there is a possibility of some back flow of blood from the pulmonary artery during the cardiotomy which could be annoying. A figure-of-eight suture is placed in the wall of the aorta in a convenient location for closing the hole made by the injection needle. The aorta and pulmonary artery are then clamped with a broad, nonerushing clamp and the calculated dose of

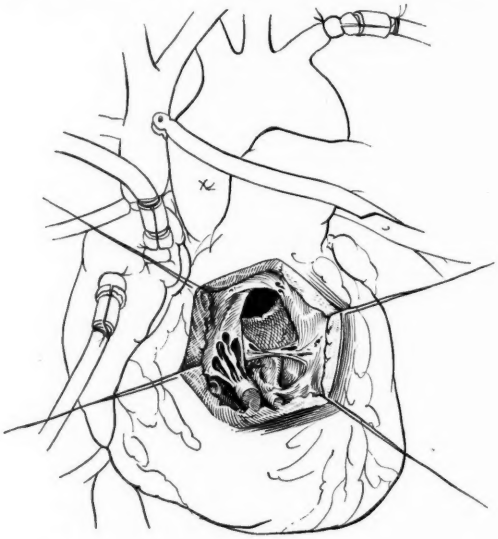


Fig. 2.—Common appearance of ventricular septal defect through right ventriculotomy.

acetylcholine (10 mg. per kilogram in 10 to 20 c.c. of saline solution) is injected rapidly into the aorta. The heart stops when about two thirds of the solution has been injected, but the injection is continued. Thereafter, the heart beats only during gross mechanical stimulation of the ventricular wall. An incision is made rapidly into the right ventricle along the outflow tract toward the pulmonary artery, avoiding branches of the coronary artery if possible and, of course, the pulmonary valve. The residual blood in the ventricle is removed by suction. If the caval cannulation and snaring has been accurate and there is no systemic drainage via the coronary sinus, there will be little blood to contend with after the original aspiration. A small amount of bright bronchial

blood escapes from the septal defect or defects, but this is more of a help than a hindrance, since it practically guarantees against air embolism and also reveals additional defects after closure of the first one.

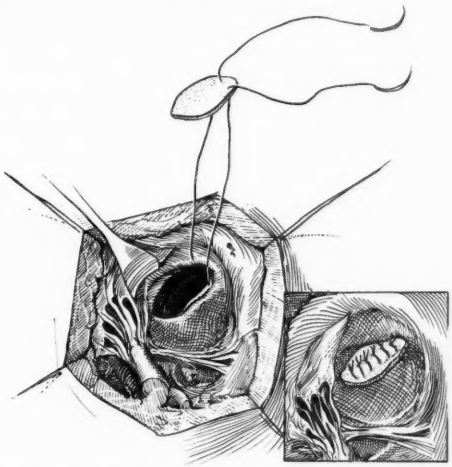


Fig. 3.—Method of closure of defect using double-armed sutures passed through a pledget of compressed Ivalon sponge. *Inset:* Completed closure of defect.

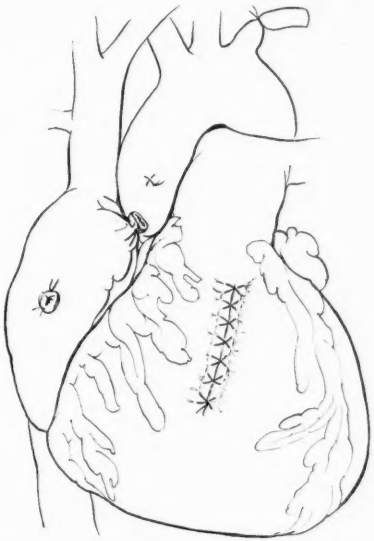


Fig. 4.—Closure of cardiotomy incision and decannulation.

In the quiet, dry heart in induced arrest, visualization and evaluation of the septal defect offer no great problem (Fig. 2). Papillary muscles have been divided in only 3 cases to obtain exposures for the suturing. Following closure

of the defect by one of the methods discussed below (Fig. 3), any papillary muscles which have been divided are repaired, and the suturing of the ventricular incision is begun inferiorly. At this point, it is desired that coronary circulation be restored so as to wash out the cardioplegic drug and restore the heartbeat. This is done simply by removing the aortic clamp. This allows the oxygenated blood from the pump-oxygenator to enter the coronary arteries, where it passes from the coronary sinus into the right auricle, thence through the tricuspid valve into the open right ventricle, where it is removed by suction until the final part of the closure of the ventricular incision (Fig. 4), at which time the heart is almost invariably beating effectively. Closure of the ventricle with air trapped inside is impossible in this situation. The electrocardiographic pattern in a typical case is shown in Fig. 5.

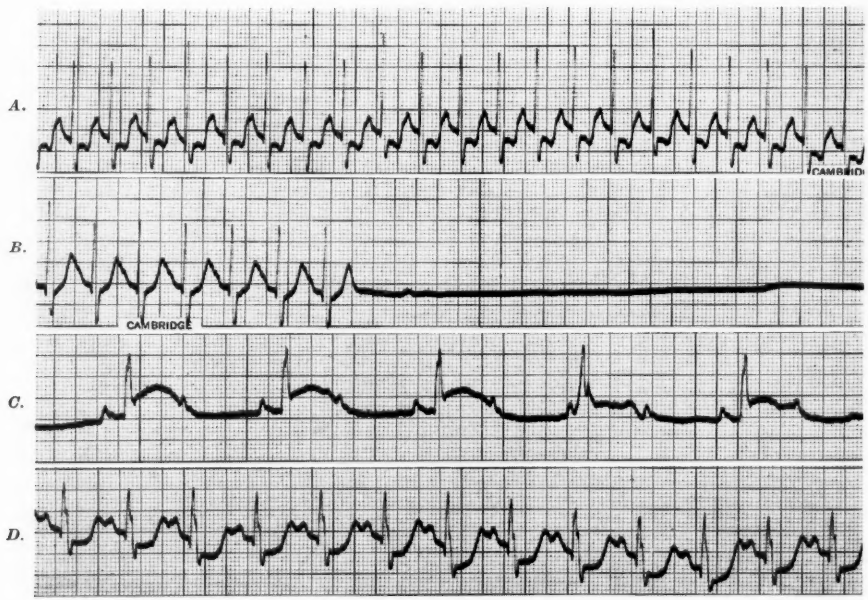
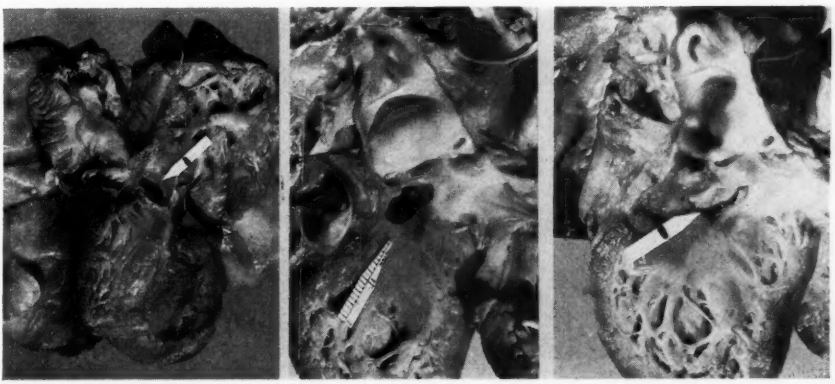


Fig. 5.—Electrocardiographic records during the closure of ventricular septal defect in a 9-year-old girl.
A, Tracing before cardiotomy.
B, Tracing showing instantaneous arrest of the heart with the injection of acetylcholine.
C, Tracing during recovery phase following removal of aortic clamp.
D, Resumption of normal rate and rhythm during closure of chest.

RESULTS OF CARDIAC ARREST AND RESUSCITATION

Following the induced cardiac arrest in the 53 operations for the repair of ventricular septal defects, the heartbeat returned in all following coronary perfusion. In 2 early cases (Nos. 4 and 8), cardiac massage was applied because of delay in the appearance of the heartbeat. This delay is now thought to be due to the inadequacy of the coronary perfusion due to the low flows

(30 c.c./Kg./min.) being used at that time. Both of these patients survived. Ventricular fibrillation appeared during the recovery phase in 3 cases. In each instance, one light countershock converted the fibrillation. Since atrioventricular block occurs in the absence of induced arrest as a result of the surgical manipulations in the conduction areas, this is not a specific complication of the arrest. It was observed in 9 cases in this series. A sinus rhythm was established late in the first postoperative day in 3 cases, one patient is alive 4 months after the operation with persistent block and 5 patients died with the atrioventricular block apparently responsible for the fatal outcome.



A. *B.* *C.*

Fig. 6.—Heart of a 7-month-old child who died of unknown cause (possibly atelectasis) 24 hours after closure of ventricular septal defect. The sutures have been removed to show the pathologic anatomy.

A, Right ventricular aspect.

B, Left ventricular aspect with defect opened by traction.

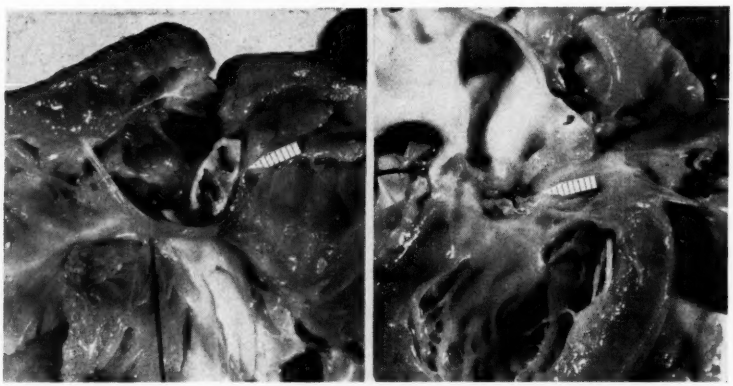
C, Left ventricular aspect with defect almost closed by gentle approximation of the edges.

TYPES OF DEFECTS AND METHODS OF CLOSURE

We have made no attempt to classify the defects according to the Rokitansky classification suggested by the Minneapolis group.[17] Suffice it to say that 52 of the 53 were high defects, and only one was a small defect low in the septum. Examination of the specimens in nonsurvivors had shown that from the left ventricular aspect, the defects appear very similar (Figs. 6 and 7). It would appear to be logical for the approximating suture line to run parallel to the annulus of the aortic valve. In no specimen was any tearing out of the sutures observed; therefore, we have not been placing a "filler" of noncompressed Ivalon sponge in the defect as suggested by Kirklin and his associates.[18] In one of the early cases (No. 11), a hasty continuous suture line was put in because of poor visibility due to excessive intracardiac blood from a temporarily overlooked left superior vena cava. The murmur reappeared on the fifth postoperative day, and a month later, a second cardiotomy was done and the suture line was found to be partially disrupted. This time, the ends of the sutures were

passed through a pledget of Ivalon sponge by means of double-armed needles and tied over this (see Fig. 3). This technique has become practically standard, and there is no further known instance of recurrence of the defect.

We have obtained a definite impression that if the sutures can be placed in white fibrous tissue rather than pink or red tissue, heart block will not be encountered. With the ideal conditions for visualization present during the induced arrest, one can pull aside the pink tissue on the right ventricular side, and usually, the whitish lining of the left ventricle comes into view to receive the sutures.



A. *B.*

Fig. 7.—Heart of 6-month-old infant who died 4 hours after closure of interventricular septal defect because of faulty blood replacement.

A, Right ventricular aspect showing Ivalon pledget in place.

B, Left ventricular aspect, showing complete closure without encroachment on the aortic valve.

At first glance, the mortality rates shown in Table I appear unreasonably high. The factors contributing to the over-all mortality rate in order of importance are: (1) 7 of the deaths were in tiny, desperately ill infants under one year of age. Two of them were under 6 months of age. Several deaths are attributable to causes which are now known to be preventable, i.e., technical errors related to the by-pass procedure and less than optimum postoperative management. Three deaths were probably due to faulty control of blood coagulation and blood replacement. Respiratory difficulty and cyanosis have appeared suddenly in several of the tiny infants, and fatal arrhythmias appeared immediately. We have recently used prophylactic tracheotomy in 2 small children with satisfaction. Bronchial aspiration can be carried out repeatedly by the nurse, and the children are relieved of the necessity of coughing to which they have little tendency.

In no instance has there been evidence that a fatal result was due to the heart having been stopped with the cardioplegic drug, unless the cases of fatal heart block can be ascribed to the heart having been still while the sutures are

TABLE I. RESULTS IN CLOSURE OF VENTRICULAR SEPTAL DEFECTS

AGE	NUMBER OF CASES	DEATHS	MORTALITY RATE (%)
All cases	53	17	32
Under 1 year	13	7	54
Over 1 year	40	10	25
Over 2 years	27	5	18
Over 3 years (Pumped 50 c.c./min.)	19	1	5

being placed. It is our impression that the incidence of the heart block is as great in the hands of surgeons who do not use induced cardiac arrest. We have not observed heart block when it has been possible to place the sutures through the whiter fibrous tissue as described above.

SUMMARY AND CONCLUSIONS

We have reported an experience with 53 operations for the closure of interventricular septal defect with the adjunct of acetylcholine-induced cardiac arrest. The use of the cardioplegic drug makes the technical aspects of the operation considerably easier, and will probably contribute to a progressive lowering of the operative mortality.

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DISCUSSION

(PAPERS BY EFFLER [PAGE 500], AND LAM [PAGE 509] AND THEIR ASSOCIATES)

DR. PETER ALLEN, Minneapolis, Minn.—The results obtained by Dr. Effler and Dr. Lam are indeed enviable. At the University of Minnesota Hospital we have not had quite the same success with the use of potassium-induced cardiac arrest. Prior to the use of this drug we repaired 165 ventricular septal defects. There were 19 cases (11.5 per cent) in which total heart block occurred. Of the 19 cases, 13 eventually died, and 5 reverted to sinus rhythm. One is still alive 10 months later with persistent heart block. Compare this with 36 cases of ventricular septal defect repaired with potassium arrest. Nine cases (25 per cent) developed persistent heart block. Of the 9, 5 have died, 4 as a direct result of the heart block and one as a result of an uncontrolled infection. Four patients are alive; 2 have spontaneously reverted to sinus rhythm, one case 1½ days following surgery and one, 7 days following surgery. Two are alive 5 months after operation, with persistent heart block, and seem to show no obvious limitation of activity.

As a consequence, then, we have used induced cardiac arrest with potassium not routinely but only in cases where it is necessary to improve the exposure. A right ventriculotomy is performed and the ventricular septum inspected; if the defect proves difficult to expose and an incomplete repair might result, only then is potassium arrest used. Therefore, on our service at the University of Minnesota Hospital, when considering potassium arrest, one must weigh the consequences of improving intracardiac exposure versus the possibility of an associated heart block and possibly death.

DR. HARRIS B. SHUMACKER, JR., Indianapolis, Ind.—I want to congratulate both Dr. Effler and Dr. Lam. We have certainly been highly pleased with the use of induced cardiac arrest, in the manner Dr. Effler has outlined, when we have employed the pump-oxygenator. The problem of cardiac arrest in the hypothermic state has proved a more formidable one than under normothermic conditions. Dr. Riberi and I have been studying this problem. I should like to show a brief movie illustrating a method which we have found satisfactory in the dog. The aorta is cannulated via the subclavian artery and its tip is made to lie in the proximal portion of the aorta. The arrest is induced with 5 meq. of potassium lactate. After one closes the heart, the aorta and coronary arteries are perfused with oxygenated blood until the heart becomes pink. Then one injects a small amount of calcium gluconate. Restoration of cardiac contractions and a normal rhythm take place quite promptly. Whether this method will have clinical applicability I do not know. As long as hypothermia is used we should have available a safe method for inducing cardiac arrest.

DR. J. L. EHRENHAFT, Iowa City, Iowa.—Much of what I wanted to say has already been said by the previous discussors. At the present time we have a smaller series of patients in whom interventricular septal defects have been repaired using an extracorporeal circuit and pump-oxygenator of the DeWall type. Our series at the present time consists of 28 patients. All of these were patients with interventricular septal defects with or without infundibular stenosis and other associated intracardiac or large vessel anomalies. We have applied the Melrose technique of cardiac arrest in about half of these patients. The decision as to whether potassium arrest should be used is usually deferred until the time the heart has been exposed and, at times, partly explored. We feel that potassium arrest

is a great adjunct in the more complicated type of defects, particularly if they are associated with infundibular stenosis or if they are of the tetralogy of Fallot type. In simple interventricular septal defects usually cardiac arrest has not been instituted and the coronary venous blood has been returned to the pump-oxygenator. We have used potassium citrate to stop the heart and have no experience with acetylcholine. The longest time of potassium-induced arrest was 32 minutes. We have had 3 deaths in this series of 28 patients, none of which could be attributed to the potassium arrest per se.

Even though it does not pertain to the two papers I am discussing, I would like to make a statement regarding cannulization of the left subclavian artery for return of blood to the aorta during the cardiopulmonary by-pass. It has been mentioned by both essayists. We have noted that in most of our patients, even though we try to be quite careful, a Horner's syndrome on the left has occurred if the left subclavian artery was used for cannulization. I do not know if this Horner's syndrome, which may be quite disfiguring in some patients, is permanent. If it should be, that may be a good reason for not using the subclavian artery for cannulization, but return the oxygenated blood to the patient via the femoral artery.

DR. JOHN E. JESSEPH, Seattle, Wash.—We have been interested in induced cardiac arrest, and our clinical experience with this technique has been rather limited. In the laboratory we have induced arrest for a period of 30 minutes and, before, during, and following the period of arrest we have studied changes in the three principal carbohydrates which serve as energy sources for an isolated, perfused heart. We have done oxygen and CO_2 studies, and have also measured pH. It is interesting to note the apparent approximation before and after arrest of the uptake of oxygen. Glucose utilization and CO_2 production are lower following arrest, probably because of a slower rate. Very fundamental to our consideration of this matter is the obvious conclusion from the tremendous outpouring of lactate during the postarrest period, that very likely the myocardium has utilized a significant quantity of its glycogen to support its energy requirements during arrest. Not shown in this slide is the fact that a 30-minute arrest period reduces the pH of the heart blood from the level of normal to 7.0 or below. I think this has a rather significant implication in terms of defining the safe limits of induced cardiac arrest and the use of this method in diseased or damaged hearts.

DR. RALPH A. DETERLING, JR., New York, N. Y.—In our laboratory, Dr. Bhonslay has conducted a study in about 250 dogs with the DeWall pump-oxygenator. Of these, 75 were to evaluate the different methods of producing cardiac arrest during extracorporeal circulation. As was shown by Dr. Effler, we succeeded with potassium citrate, using 300 to 400 mg. However, we had a number of dogs in which the heartbeat could not be maintained well after total arrest of the heart for about 30 minutes. Acetylcholine, and an English drug, Moryl, which resembles acetylcholine, also were tried but the effect usually fell short of complete arrest. With these two agents, electrical activity was still evident by electrocardiogram, and the myocardium responded to minimal stimulation.

We would like to call your attention to the fact that simple cardiac anoxia produced by clamping of the aorta during extracorporeal circulation can initiate satisfactory arrest. For several minutes the electrocardiogram remains nearly normal although the heartbeat weakens appreciably and then stops. Upon releasing the clamp, the myocardium becomes pink immediately, and a good cardiac beat develops. We have had one patient with transient ventricular fibrillation after removal of the clamp. This arrhythmia converted spontaneously to a strong regular beat within 10 minutes during closure of the right ventricle. With regard to time, we have used potassium-induced arrest for one hour with recovery of good heart action in 3 children. These patients did not survive, however, having had very complex and severe anomalies. We believe on the basis of our animal work that the use of the anoxia technique may be as good as or superior to the use of potassium citrate or acetylcholine. I was interested to note that this technique has been employed successfully by DeBakey's group during excision of aneurysm of the ascending thoracic aorta.

DR. CHARLES P. BAILEY, Philadelphia, Pa.—We were late at our clinic in adopting cardioplegia for open-heart surgery, largely, I think, because we hate to see the heart stop beating. Both Dr. Effler and Dr. Lam have tried previously to point out the error of our ways, without success for awhile. One phase of open-heart surgery which has not been stressed, although mentioned by Dr. Effler, is open-heart surgery for aortic stenosis, following the lead of Lewis and Lillehei. We have now operated on more than 40 patients by that technique, and we have been greatly troubled by the fact that, when you open the aorta, the ventricles tend to fibrillate. If you use hypothermia the patient may get by, but if the heart should fibrillate then you will have a lot of trouble getting the heart back into sinus rhythm.

We have used the method suggested by my associate, Dr. Gumersindo Blanco, of perfusing the coronary sinus in retrograde fashion. Some of the patients are greatly protected by this technique. However, it is a bit irregular in its action and some of them fibrillate very quickly. We think this is due to variations in the pattern of the tributaries of the coronary sinus. So we have finally come to induced cardiac arrest using potassium citrate, as the best method to prevent this complication. We have had no difficulty in restoring cardiac action after its use.

DR. DONALD B. EFFLER., Cleveland, Ohio (Closing).—I would like to thank the discussants for their contributions and for their interest in this subject.

As a matter of record, I have no desire to quarrel about priority in the use of elective cardiac arrest. It is our desire to point out one method of inducing cardiac arrest as it was suggested by Melrose and his associates; actually this work had been suggested many years ago and has had clinical application in this country by Swan and others using hypothermia. It is our opinion, however, that Melrose and his associates must receive credit for its application in the field of open-heart surgery employing the cross-circulation technique.

Dr. Allen has mentioned the problem of heart block following open cardiotomy with the pump-oxygenator. We have been singularly fortunate in that heart block has not been a serious problem in our experience and its rate of occurrence has been low. I do not believe that heart block is produced or aggravated by elective cardiac arrest; for that matter I do not believe that it must always be explained by ligation of conduction bundles by the inadvertently placed suture. There is evidence to suggest that heart block occurs in a sick heart that is subjected to trauma and to localized myocardial anoxia. However, that is not completely settled by any means.

I appreciate the comments made relative to the effects of hypothermia. We try our best to avoid it; however, as Dr. Shumacker has stated, hypothermia will occur particularly in the younger patients, in spite of all precautions.

I would like to thank Dr. Bailey for his comments relative to elective cardiac arrest in the surgical treatment of aortic stenosis. I hope that his enthusiasm will persist with the passage of time. As mentioned earlier, our enthusiasm for elective cardiac arrest as an adjunct to open-heart surgery has persisted to the present time. However, things change rapidly and by next year we may have a different story.

Again, I would like to thank the Association for the opportunity of presenting this paper.

DR. CONRAD R. LAM, Detroit, Mich. (Closing).—I too would like to thank the discussants. I must admit that the results we reported on isolated interventricular septal defects are the best of the story. Our experience with the other lesions will have to be reported separately. The problem of stopping the hypertrophied heart, such as one with aortic stenosis, and particularly the one with aortic regurgitation, is very complicated. When acetylcholine is injected into the aorta in such a case, it does not go into the coronary arteries; it goes down into the left ventricle through the incompetent valve. There are a great many more problems which have to be solved.

To Dr. Effler belongs the credit of the first deliberate and successful stopping of the human heart for an intracardiac surgical procedure.

TOTAL GASTRECTOMY: TWO CASE REPORTS INTRODUCING THE USE OF TWO LEVIN TUBES FOR BOTH ASPIRATION AND FEEDING PURPOSES

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SINCE most authors ascribe surgical mortality in total gastrectomy to an anastomotic leak, we are introducing the use of two Levin tubes; one ending in the distal jejunum for feeding purposes, the other ending in the duodenal stump or proximal jejunum for suctioning purposes in order to prevent increased intraluminal pressure. As was shown by Gatch,[1] this pressure can in itself cause venous occlusion with the beginning of an irreversible chain of events, which may eventually lead to anastomosis disruption followed by peritonitis or pleuritis as the case may be. The Levin tubes are used not only to prevent increased intraluminal pressure and the subsequent blowing out of any anastomotic areas but also to make certain that no stenosis at any of the anastomotic sites occurs. This is true of the Roux Y technique of total gastrectomy, and also for any subtotal gastrectomies which leave a duodenal stump. Many authors have intubated the distal jejunum for feeding purposes or the proximal jejunal stump for aspiration (Strode,[5] Palumbo and Brennan,[3] ReMire and Priestley,[4] and Kline[2]), but no one has intubated both the proximal and distal loop simultaneously as is advocated in this article.

CASE REPORTS

The following 2 cases of total gastrectomy illustrate the use of two Levin tubes.

CASE 1.—Patient C. F. was a 71-year-old Japanese man whose chief complaint was epigastric fullness which had been present for two months. For two months prior to admission to the hospital, the patient had noticed that his food did not taste as good as it did previously. He was, also, able to eat but very small quantities of food. He had a sensation of fullness which had become progressively worse. There had not been any pain, belching, or constipation. He had never vomited or noticed any blood, either bright or dark, in his stools. Anorexia had become progressively worse, so that at the time of admission the patient had no appetite whatsoever. The patient stated that during the two months prior to hospital admission, he had lost a total of 13 pounds in weight.

Physical examinations disclosed a 71-year-old Japanese man who did not appear chronically ill. Complete routine physical examination was essentially normal except for the fact that the abdominal veins were unusually prominent and there was muscle guarding in both the right and left upper quadrants of the abdomen.

Received for publication Nov. 29, 1956.

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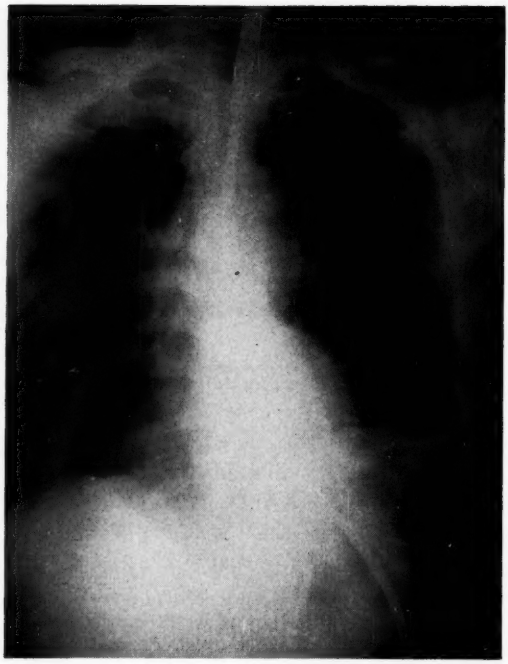

Fig. 1.—X-ray showing 2 Levin tubes in esophagus and proximal and distal jejenum.

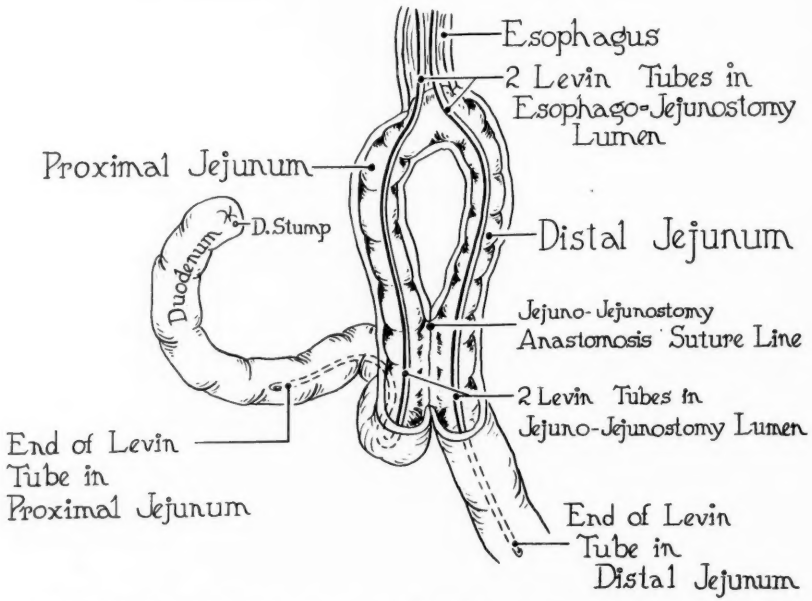

Fig. 2.—Drawing which shows the use of 2 Levin tubes in one of the cases reported.

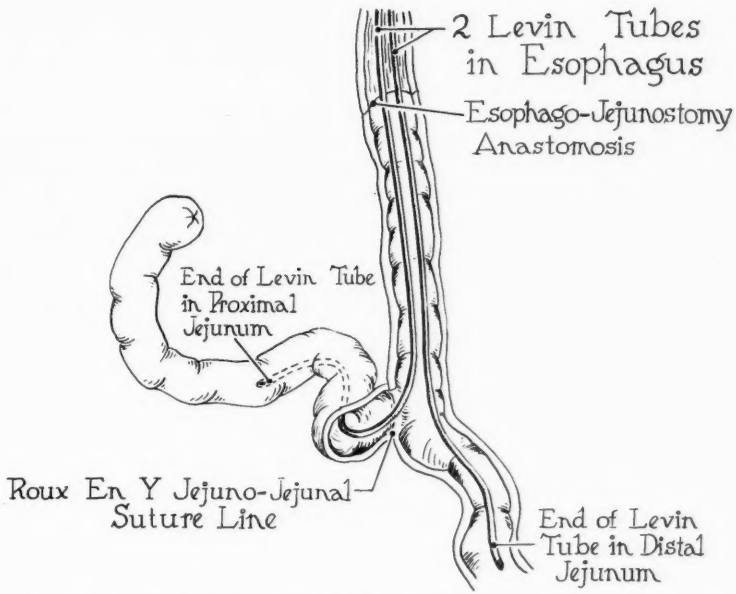

Fig. 3.—Drawing which shows use of 2 Levin tubes in Roux Y total gastrectomy.

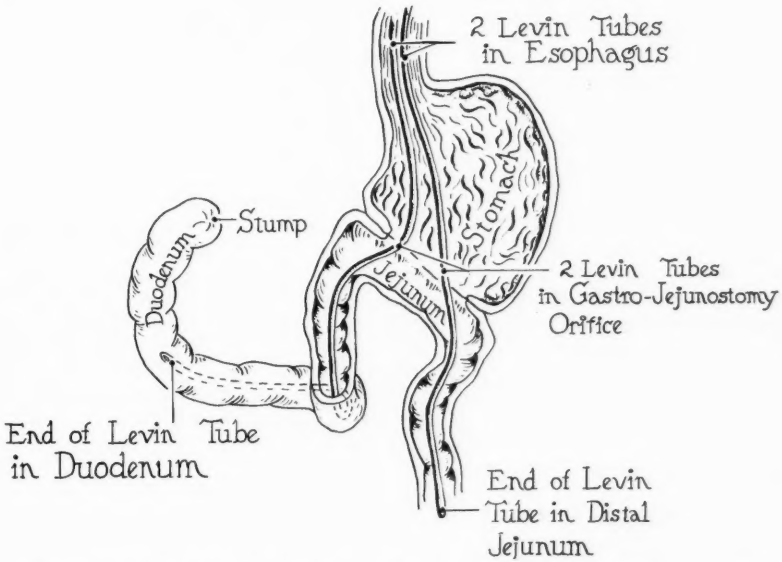

Fig. 4.—Drawing which shows the use of 2 Levin tubes in subtotal gastrectomy.

Preoperative x-rays showed a very extensive ulceration in the fundus of the stomach with a loss of the normal mucosal pattern and with narrowing of the stomach size all the way from the esophagus to the duodenum. The preoperative diagnosis was, "Carcinoma of the stomach, probably linitis plastica."

Exploratory operation was performed, utilizing a transthoracic approach, on July 1, 1953. The stomach was almost completely replaced by an obstructing linitis plastica; frozen sections of lymph nodes in both the greater and gastrohepatic omentum showed a wild anaplastic carcinoma. Accordingly, the simplest possible palliative operative procedure was performed—a total gastrectomy. After the esophagojejunostomy anastomosis was completed, one of the two Levin tubes which had been placed in the esophagus, previously, was threaded down for a distance of at least 3 inches beyond the distal portion of the jejunojejunostomy into the distal jejunum. The other tube was inserted into the duodenum. The tubes were marked for identification. Immediate suctioning was applied to the distal and proximal jejunal loops, and small amounts of feedings were given very early through the tube in the distal loop; whereas the tube in the proximal loop was designed to be used essentially for aspiration purposes. Both tubes were easily removed by rotation on the eighth day when the patient had good peristaltic sounds, a soft flat abdomen, formed stools, and was eating by mouth without difficulty.

The patient was ambulatory by the eleventh postoperative day and was discharged from the hospital. He was able to eat well—eating four good-sized meals a day. He had essentially normal bowel movements and, until his death approximately six months after surgery, his weight remained almost constant. Autopsy showed that the esophagojejunal anastomosis was patent, but metastatic lesions were present in the omentum and bowel.

CASE 2.—Patient F. M. was a 64-year-old white woman who had had gastroscopy performed in 1952 because of tarry stools. A diagnosis of gastric ulcer was made. She had had infrequent care until August, 1954, when she had developed anorexia and persistent abdominal pain. A repeat gastroscopy showed considerable tumor filling most of the stomach. She had lost 32 pounds in two years. Examination disclosed a woman who exhibited considerable evidence of weight loss and a slightly tender mass in the epigastrium.

On Dec. 29, 1954, a palliative total gastrectomy was performed since the stomach was almost completely replaced by adenocarcinoma and clearance sections of the esophagus and duodenum showed involvement of muscularis by the carcinoma. Prior to completion of the jejunojejunostomy, two Levin tubes were passed through the esophagojejunal opening; a rubber tube into the proximal jejunal loop and a plastic tube into the distal jejunal loop. For the first two days constant suction was applied to the proximal tube and the bile drainage was injected into the distal jejunal tube. Both tubes were irrigated with normal saline frequently. Feedings were given through the distal tube. After good peristaltic sounds were present and the abdomen was soft and flat, the proximal tube was removed. The patient developed a left subphrenic accumulation of fluid which communicated with the pleural space so that it was necessary to remove it by thoracentesis. The distal tube was removed later, on Jan. 10, 1955, after she was able to take food by mouth.

She had an uneventful convalescence, maintaining her weight until Feb. 8, 1956, at which time she was readmitted to the hospital for intestinal obstruction due to a large firm metastatic lesion which occluded the lumen of the splenic flexure of the colon. A transverse colostomy was done, and the patient was discharged in a markedly improved condition on the thirteenth postoperative day.

SUMMARY AND CONCLUSIONS

Two cases of total gastrectomy are reported introducing the use of two Levin tubes in order to reduce the morbidity and mortality. The proximal tube is for suctioning of the proximal jejunum and duodenal stump in order

to prevent increased intraluminal pressure and thus preventing leakage or blowout of the duodenal stump. The distal tube is for feeding purposes in the distal jejunum beyond the anastomotic site.

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EXPERIMENTAL STUDY OF TRACHEAL RECONSTRUCTION

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ALTHOUGH in surgery on the respiratory organs the technique of pulmonary resection has been almost perfected, surgical treatment of the trachea and bronchus, especially tracheal reconstruction of large defects following tubular resection, still needs improvement.

According to a review of the literature, tracheal and bronchial surgery was reported for the first time by Gluck in 1899.[12] Later research has been devoted chiefly to the cervical trachea, but since 1948 operative intervention for repair of the thoracic trachea has been attempted. Ferguson,[7] Meyer,[16] Kiriluck,[15] Gebauer,[10, 11] Paulson[18] and their associates have reported fairly good results in recent years with direct anastomosis. In the repair of partial tracheal or bronchial defects with other tissues, fascia,[20] pericardium,[14] chest wall,[19] and others have been used as well as the well-known Gebauer dermal graft supported by wire. Experimentally and clinically, the results were fairly good.[8, 9]

Various methods of restoring tubular tracheal defects with other materials have been tried, but without satisfactory results. For the prosthesis, Daniel[4, 5] used glass, stainless steel, Vitallium, and plastics, while Clagett[2] and Craig[3] employed polyethylene tubes, and Bucher[1] made use of stainless steel wire mesh. Hukuda[12] used heterogenous arterial graft supported with wire. O'Brien,[13] Davies,[6] Hukuda,[12] and Nishi[17] reported on homogeneous tracheal graftings, and Clagett and others[2] used tantalum mesh with a temporary prosthesis of polyethylene tube.

Although many authors reported a surgical technique for trachea and bronchus, we consider it more practical to reconstruct the tubular resected trachea with a material which is as near to the normal tracheal structure as possible. We attempted to reconstruct a trachea that would be flexible and elastic and, moreover, in which stenosis would not occur. To maintain an airway and prevent infection, as well as air leak, a polyethylene tube was inserted temporarily as a prosthesis, until the transplanted grafts had conglutinated. The results of our experiments did not meet our expectations. It is believed, however, that a practical method of reconstructing the trachea has been attained and the present paper is to report the methods used and the results.

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Received for publication Dec. 3, 1956.

METHODS

A polyethylene tube supported with stainless steel wire, made for the purpose, was used. Various-sized tubes, 1.8, 1.6, 1.4, 1.2, 1.0 cm. in diameter, were prepared, in order to have one suitable for any given case (Fig. 1). These tubes were stored in 70 per cent alcohol.

Adult mongrel dogs, weighing between 8 and 14 Kg., were used. For anesthesia, 20 to 30 minutes after subcutaneous administration of 2 per cent morphine hydrochloride, hexobarbital sodium (Evipal) is used intravenously for induction. An endotracheal tube is intubated and a closed circuit system is established. Anesthesia is maintained with oxygen and ether or with oxygen and hexobarbital sodium. The skin incision is made along the right third rib, about 8 cm. long, in lateral position. Thoracotomy is done by resection of the right third rib. Following infiltration of 2 per cent Novocain around the vagus nerve, the right subclavicular vein is ligated and divided and the trachea is

Fig. 1.—Polyethylene tube supported with wire.

exposed freely and cut at the prearranged distal line. Another intratracheal catheter is inserted into the tracheal stump and the airway is secured. Then a portion of trachea is removed, approximately 3 to 5 cm. long, toward the oral side from the line of division. This tubular defect is then restored with a polyethylene tube of proper size. Fixation of the tube to the trachea is made at each end of the tube with silk, and approximation of the overlapped trachea and the tube is made tight by catgut or silk (Fig. 2). On the exposed surface of the tube various autografts are transplanted annularly without fixation to any other tissue. The silks or catgut, approximating the two ends of the tube to the cut trachea, are tied together over the right and left mid-portions of the graft to prevent abnormal gaping of the divided trachea. After absence of air leak from the transplanted portion has been affirmed by elevation of the endotracheal pressure, the mediastinal pleura is closed following an injection of penicillin into the mediastinum and pleural cavity. The pleural cavity is closed without drainage.

All animals received 300,000 units of penicillin daily for two days after the operation. The indwelling polyethylene tube was removed after a definite period by means of a forceps under bronchoscopy.

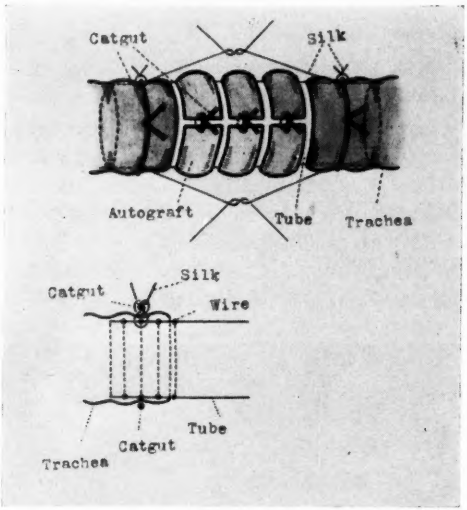

Fig. 2.—Autografting with a polyethylene tube prosthesis.

RESULTS

A. *Autografts of Laminated Costal Cartilage.*—Twenty dogs were used for this experiment. Standard skin incision was extended 7 to 8 cm. long to the abdominal side in hook shape about 1 to 2 fingerbreadths from the parasternal line. The tissues to be used for autografts were split with a knife, 2 to 3 mm. in thickness, 5 to 8 mm. in width, and 5 to 6 cm. in length, from the external layers of the third, fourth, and fifth costal cartilages with perichondrium. Three grafts were fixed annularly on the exposed surface of the polyethylene tube. Tubes were removed 2 to 14 weeks after operation. Table I shows the cause of death in

TABLE I. CAUSE OF DEATH BEFORE REMOVAL OF THE TUBE: AUTOGRAFTS OF LAMINATED COSTAL CARTILAGE

CASE NO.	PERIOD OF SURVIVAL	CAUSE OF DEATH
13	Just after operation	Operative and anesthetic death
22	8 hours	Operative and anesthetic death
29	Just after operation	Operative and anesthetic death
39	Just after operation	Operative and anesthetic death
41	5 hours	Operative and anesthetic death
19	1 month	Pneumonia
21	15 days	Pneumonia
18	1 month	Pyothorax
17	2 months	Hanging
20	6 months	General weakness

10 dogs which died before removal of the tubes. Tubes were removed in 10 dogs, 8 of which died apparently of tracheal stenosis. Of 8 dogs in which tubes

were removed 6 to 14 weeks after operation, 7 died within 2 weeks following the removal of the tubes, exclusive of one, which survived 3½ months after removal. In 2 cases in which the tubes were removed 2 weeks after operation, there was no perforation and one of the dogs survived 4 months (Table II).

TABLE II. COURSE AFTER REMOVAL OF THE TUBE: AUTOGRAFTS OF LAMINATED COSTAL CARTILAGE

CASE NO.	PERIOD UNTIL REMOVAL OF THE TUBE (WEEKS)	PERIOD OF SURVIVAL AFTER REMOVAL OF THE TUBE	DEGREE OF TRACHEAL STENOSIS	CAUSE OF DEATH
8	12	5 hours	+++	Tracheal stenosis
23	14	8 hours	+++	Tracheal stenosis
24	7	11 days	+++	Tracheal stenosis
25	7	3 days	+++	Tracheal stenosis
26	6	10 days	+++	Tracheal stenosis
27	6	3 days	+++	Tracheal stenosis
38	2	4 months	+++	Tracheal stenosis
40	2.5	10 days	+++	Tracheal stenosis
14	10	7 days	+	Pneumonia
16	10	3.5 months	+	General weakness

Since this seemed to indicate that the tubes could have been removed with good results about 2 weeks after operation, in the subsequent experiments 2 weeks were set as the approximate time of removal.

The bronchoscopic findings after removal of the tube disclosed the fact that the more profuse the discharge with coating, the stronger was the tendency toward tracheal stenosis. In macroscopic findings of the transplanted portion at autopsy, all cases showed no perforation and the transplanted cartilages were definitely recognized grossly. In those cases in which the tubes were not removed, tracheal stenosis had not occurred, but in the cases in which the tubes were in place for a long time after operation, there was an increased thickness of the wall and it was presumed that tracheal stenosis was likely to occur soon after removal of the tube. In 8 cases of tracheal stenosis, the wall was 5 to 8 mm. thick. Five cases of tracheal stenosis were due to abnormal fibroplasia and 3 to cicatricial constriction.

Microscopically, partial epithelization was found in 3 cases. In these cases, inflammatory processes were less marked than in cases of nonepithelization, and tracheal stenosis, which resulted in death, was found to be due to cicatricial constriction. Grafts were retained in all cases with one exception. In 7 cases, absorption and necrosis of grafts were recognized, and in 6 cases grafts were exposed to the internal surface of the tracheal lumen.

B. *Autografts of Whole Costal Cartilage.*—Twenty-three dogs were used for this purpose. The skin incision was made parallel to the midline and 3 to 4 fingerbreadths from the right sternal margin at the level of the tenth to twelfth ribs. The twelfth, eleventh, and tenth costal cartilages were removed. When the twelfth costal cartilage was too short, the ninth costal cartilage was tried. After the incised wound had been closed, the trachea was removed as just described. Three grafts were transplanted annularly on the exposed surface of

the tube. Tubes were removed 10 to 18 days after operation in accordance with our experience with Group A. Four dogs died before removal of the tubes (Table III). Tubes had been removed in 19 cases and 8 of the dogs died of

TABLE III. CAUSE OF DEATH BEFORE REMOVAL OF THE TUBE: AUTOGRAFTS OF WHOLE COSTAL CARTILAGE

CASE NO.	PERIOD OF SURVIVAL (DAYS)	CAUSE OF DEATH
46	Just after operation	Tension pneumothorax
86	7	Tension pneumothorax
64	18	Tracheal obstruction (sliding of the tube to the pulmonary side)
43	3	General weakness

tracheal stenosis. Five dogs died of pneumonia, 2 of tracheal obstruction, and 4 of general weakness. The longest survival period was one year following the operation, which was 11½ months after removal of the tube. Six dogs lived longer than 3 months and 3 survived longer than 6 months (Table IV).

TABLE IV. COURSE AFTER REMOVAL OF THE TUBE: AUTOGRAFTS OF WHOLE COSTAL CARTILAGE

CASE NO.	PERIOD UNTIL REMOVAL OF THE TUBE (DAYS)	PERIOD OF SURVIVAL AFTER REMOVAL OF THE TUBE	DEGREE OF TRACHEAL STENOSIS	CAUSE OF DEATH
44	16	2.5 months	+++	Tracheal stenosis
47	17	8 days	+++	Tracheal stenosis
49	16	3 months	+++	Tracheal stenosis
65	18	10 days	+++	Tracheal stenosis
69	11	1 month	+++	Tracheal stenosis
71	17	3 months	+++	Tracheal stenosis
87	10	2 months	+++	Tracheal stenosis
105	15	2 months	+++	Tracheal stenosis
50	14	5 hours	+	Tracheal obstruction
66	18	3 months	++	Tracheal obstruction
67	18	3 weeks	++	Pneumonia
70	17	12 days	++	Pneumonia
84	13	6 days	+	Pneumonia
85	13	8 days	+	Pneumonia
88	15	1 month	++	Pneumonia
42	14	8 months	+	General weakness
45	16	2 months	+	General weakness
48	16	6 months	+	General weakness
68	11	11.5 months	-	General weakness

The more profuse the discharge and the heavier the coating as revealed by bronchoscopic findings, the stronger was the tendency toward tracheal stenosis. Moreover, many dogs died of complications such as pneumonia at an early stage.

At autopsy, no sign of perforation was seen, exclusive of 2 of the cases of tension pneumothorax, and transplanted cartilages were found grossly in all cases. The thickness of the tracheal wall in the animals that died of tracheal stenosis was 4 to 8 mm., while some dogs having a 5 to 6 mm. thickness of the tracheal wall showed no stenosis. One dog that survived 11½ months after removal of the tube showed no signs of stenosis (Fig. 3).

Microscopically, epithelization was found in one case of survival of 8½ months after operation. In this case there was less evidence of cell infiltration, with no sign of absorption and necrosis in the transplanted grafts, and fibroplasia was scarcely seen; thus no scar tissue formation was to be seen, but the epithelization was only partial (Fig. 4). Transplanted costal cartilages were found in all cases, but in 16 absorption and necrosis were found. In 8 cases, grafts were exposed on the internal surface of the tracheal lumen.

Fig. 3.—A specimen of whole costal cartilage grafting, 11½ months after removal of the tube, shows no tracheal stenosis.

C. *Autografts of Costal Periosteum.*—Seventeen dogs were used. The skin incision was made similar to that in the cases of laminated cartilage grafting. In these dogs, the external half of the costal periosteum of the third, fourth, and fifth ribs was split, 5 to 6 cm. long and 5 to 8 mm. in width. Three grafts were transplanted on the exposed surface of the tube, restoring the defect of the trachea. Tubes were removed in 2 weeks to 4 months, taking into consideration the period of bone formation from the periosteum. Ten dogs died before removal of the tube. The causes of death are demonstrated in Table V. In 7

TABLE V. CAUSE OF DEATH BEFORE REMOVAL OF THE TUBE: AUTOGRAFTS OF COSTAL PERIOSTEUM

CASE NO.	PERIOD OF SURVIVAL	CAUSE OF DEATH
30	During operation	Operative and anesthetic death
36	During operation	Operative and anesthetic death
103	3 days	Mediastinitis
31	3 months	Pneumonia
52	9 days	Pneumonia
53	13 days	Pyothorax
51	9 days	Pyothorax
28	2 months	Tracheal obstruction
93	7 days	Tension pneumothorax
33	6 weeks	General weakness

dogs, the tubes were removed and all of the animals died of tracheal stenosis, as Fig. 5 shows. The longest survival period after removal of the tube was 6 weeks (Table VI.).

Fig. 4.—Photomicrograph of whole costal cartilage grafting, eight months after removal of the tube, showing existence of transplanted costal cartilage. (×50.)

Bronchoscopic findings, soon after removal of the tubes, showed stenotic signs already present in 5 of 7 cases. In one case in which the tube was removed 3 weeks after operation, a graft protruded into the tracheal lumen and a portion of the former graft was removed. As it showed a bonelike consistency, it should be assumed that the bone tissue had formed from the transplanted costal periosteum.

At autopsy, there was only one instance of perforation at the transplanted site. In one animal that died two months after operation and before removal of the tube, tracheal stenosis had developed due to slipping of the tube toward the oral side. Eight dogs, including this one, died eventually of tracheal stenosis; the thickness of the walls in these cases was 4 to 8 mm.

Microscopically, existence of grafts was observed in 7 cases and 5 of them revealed formation of osteoid tissue (Fig. 6). Two of them showed indications

TABLE VI. COURSE AFTER REMOVAL OF THE TUBE: AUTOGRAFTS OF COSTAL PERIOSTEUM

CASE NO.	PERIOD UNTIL REMOVAL OF THE TUBE	PERIOD OF SURVIVAL AFTER REMOVAL OF THE TUBE	DEGREE OF TRACHEAL STENOSIS	CAUSE OF DEATH
32	4 months	6 weeks	+++	Tracheal stenosis
90	17 days	3 weeks	+++	Tracheal stenosis
91	17 days	11 days	+++	Tracheal stenosis
92	22 days	14 days	+++	Tracheal stenosis
100	15 days	4 weeks	+++	Tracheal stenosis
101	15 days	3 weeks	+++	Tracheal stenosis
102	15 days	6 days	+++	Tracheal stenosis

of bone-tissue formation 3 weeks after transplantation. Partial epithelization was seen in 2 cases. It appears that the stronger the inflammatory signs, the more marked was the tendency toward tracheal stenosis, as shown in the costal cartilage grafting. In the costal periosteal grafting, scar-tissue formation tended to be less, partly because of death at an earlier stage, when compared with that in costal cartilage grafting.

Fig. 5.—Specimen of costal periosteal grafting 2 weeks after removal of the tube. The animal died of tracheal stenosis.

D. *Autografts of Rib.*—Twenty-three dogs were used. The standard skin incision was made. After the pleural cavity was opened in the second and third intercostal spaces, the third rib was resected, about 5 to 7 cm. in length, with its periosteum. The removed rib was cut lengthwise in two. These grafts were transplanted annularly on the exposed surface of the tube, so as to come in contact with the periosteal surface of the grafts. Tubes were removed 2 to 3 weeks after operation in view of the costal cartilage grafting. Six dogs died before removal of the tubes (Table VII). Tubes were removed in 17 cases and 7 of the dogs died, apparently of tracheal stenosis. Other causes of death were

Fig. 6.—Photomicrograph of costal periosteal grafting, 3 weeks after transplantation, showing formation of osteoid tissue from periosteum. (×50.)

Fig. 7.—Specimen of rib grafting, 3 months after removal of the tube, showing no tracheal stenosis.

TABLE VII. CAUSE OF DEATH BEFORE REMOVAL OF THE TUBE: AUTOGRAFTS OF RIB

CASE NO.	PERIOD OF SURVIVAL	CAUSE OF DEATH
77	During operation	Operative and anesthetic death
80	During operation	Operative and anesthetic death
74	Just after operation	Tension pneumothorax
57	5 days	Tracheal obstruction
78	4 days	Tracheal obstruction
55	6 days	Pneumonia

either tracheal obstruction, pulmonary gangrene, or general weakness. Some of them showed no tracheal stenosis as seen in Fig. 7. The longest period of survival to date is 1½ years. Five dogs lived longer than 6 months (Table VIII).

Fig. 8.—Photomicrograph of rib grafting, 6 weeks after removal of the tube, showing existence of transplanted rib and partial epithelization. (×50.)

Bronchoscopy performed just after removal of the tube showed tracheal stenosis in 2 cases only, and the relation between the stenosis and the coating or discharging was not quite as evident as in the costal cartilage grafting. The one animal that is still living 1½ years after operation showed no sign of tracheal stenosis on bronchoscopic examination.

TABLE VIII. COURSE AFTER REMOVAL OF THE TUBE: AUTOGRAFTS OF RIB

CASE NO.	PERIOD UNTIL REMOVAL OF THE TUBE (DAYS)	PERIOD OF SURVIVAL AFTER REMOVAL OF THE TUBE	DEGREE OF TRACHEAL STENOSIS	CAUSE OF DEATH
54	20	14 days	+++	Tracheal stenosis
56	19	5.5 months	+++	Tracheal stenosis
58	14	4 weeks	+++	Tracheal stenosis
75	17	7 weeks	+++	Tracheal stenosis
81	14	5 weeks	+++	Tracheal stenosis
82	14	5 weeks	+++	Tracheal stenosis
83	11	9.5 months	+++	Tracheal stenosis
60	11	8 hours	+	Tracheal obstruction
61	23	8 weeks	++	Pulmonary gangrene
59	16	6 weeks	-	General weakness
73	16	5 weeks	-	General weakness
76	16	3 months	+	General weakness
79	18	6 weeks	+	General weakness
72	16	9.5 months	-	General weakness
104	22	3.5 months	+	General weakness
62	16	1 year	+	Sacrified
63	16	1.5 years	-	Still living

Autopsy revealed no perforation, exclusive of a case of tension pneumothorax. Grossly, the transplanted ribs were recognized in all cases. Thickness of the stenosed tracheal wall was 4 to 8 mm. In 2 cases, tracheal stenosis occurred, apparently due to lack of supporting strength, as the result of broken grafts in one and to tissue destruction by severe infection in another.

Microscopically, the existence of grafts was recognized in all cases. Absorption and necrosis of the grafts were seen in 8 cases and exposure of the grafts into the tracheal lumen was present in 7 cases. Epithelization was recognized by bronchoscopy in one which survived, but microscopically only 2 cases presented partial epithelization. Of the 7 animals that died of tracheal stenosis, four deaths were due to abnormal fibroplasia and three to cicatrized constriction.

DISCUSSION

Technically, it is difficult to sew skin or fascia grafts to the cut ends of the trachea without having air leak. It is easy, however, to join both cut ends of the trachea without air leak by using a prosthesis, as has been proved in our experiments. Previously, Gebauer[9] mentioned that it was "available and simple" to perform reconstruction of the trachea with a prosthesis, but the results were not so desirable. In fact, this method was tried in both animal and man, but its long-term results were unsatisfactory, due to tracheal stenosis caused by the prosthesis falling off or due to tracheal obstruction caused by slipping of the prosthesis. Clagett and his associates used a prosthesis and covered it with tantalum mesh, ensuring the airway by the tantalum mesh after removal of the prosthesis. The disadvantage of this method, however, is that tantalum mesh is a foreign body and the reconstructed trachea is not of anatomic structure. We reasoned that the reconstructed trachea might be made more

nearly like the anatomic structure by the use of autografts, such as laminated costal cartilage, whole costal cartilage, costal periosteum, or rib for the supporting materials.

In our experiments the transplanted autografts fused with each other and it was impossible to recognize each transplanted graft ring. The transplanted portion became like an iron pipe and was therefore still far from the ideal of a flexible and elastic trachea. An absolute necessity for tracheal reconstruction is to keep the tracheal lumen of normal size in order to prevent tracheal stenosis. Prevention of stenosis is of great importance, and from our experiments inadequate support of the grafts and narrowing of the tracheal lumen by abnormal fibroplasia seemed to be the chief causes of tracheal stenosis.

From this point of view, rib grafting showed the best results. Existence of transplanted rib grafts was well recognized macroscopically as well as microscopically, and bronchoscopy revealed no tracheal stenosis in one case after 1½ years. Five dogs survived longer than 6 months and in the 2 animals that died before 6 months, autopsy revealed no tracheal stenosis.

The whole costal cartilage graft is second to the rib according to the results obtained. The longest period of survival up to the present is 11½ months after removal of the tube and a year after operation. There were 6 dogs that lived longer than 3 months after removal of the tube and 3 that survived longer than 6 months. Transplanted costal cartilages were present either macroscopically or microscopically.

Laminated cartilage and costal periosteum grafts gave inadequate support. In cases of costal periosteum grafting, though formation of osteoid tissue was recognized bronchoscopically or microscopically three weeks after grafting, all animals died of tracheal stenosis in a short time after removal of the tube. In cases of laminated costal cartilage grafting, the longest period of survival after removal of the tube was 4 months. Of 10 cases in which the tubes were removed, 8 dogs died of tracheal stenosis at even relatively earlier stages.

Concerning the problem of narrowing and obstruction of the tracheal lumen due to abnormal proliferation of connective tissue, the more severe the infection or inflammation (confirmed bronchoscopically, macroscopically, or microscopically), the more marked was the tendency toward tracheal stenosis. Tracheal stenosis occurred even in cases in which there was adequate supporting strength, such as with rib or whole costal cartilage, and was due to abnormal fibroplasia. Also, many deaths were due to pneumonia, pulmonary gangrene, pyothorax, or mediastinitis. From the above observation, it should be possible to obtain still better results by keeping infection to the minimum with adequate chemotherapy, and by limiting the formation of abnormal fibroplasia with the use of either ACTH or cortisone.

SUMMARY

1. Reconstruction of the trachea by transplantation of laminated costal cartilage, whole costal cartilage, costal periosteum, or rib has been tried by use of a temporary prosthesis of a polyethylene tube, made specially for the purpose.

2. This method was found easier technically and did not cause air leak.

3. Tracheal stenosis seems to be due to inadequate support of the grafts and the formation of abnormal fibroplasia.

4. Bronchoscopy and autopsy, as well as histologic examination, substantiated the fact that the stronger the process of infection or inflammation, the greater was the tendency toward formation of abnormal fibroplasia.

5. Long-term results were influenced by the supporting strength of the grafts. The rib grafting with the best supporting strength showed the best results. Five animals with rib grafting showed a survival period of more than 6 months, and one dog, which is still living after 1½ years, no tracheal stenosis has developed. Next to the rib in efficacy was the whole costal cartilage. The laminated costal cartilage and the costal periosteum, weaker in supporting power, were found to be unsatisfactory.

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TEN-YEAR SURVIVAL OF METASTATIC PULMONARY CHORIOCARCINOMA FOLLOWING BILOBECTOMY

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THE incidence of demonstrated pulmonary metastases from choriocarcinoma of the uterus is approximately 55 per cent according to Novak and Seah.[3] That this is of great prognostic significance is evidenced by the fact that only 2 patients in 41 with metastases to the lung, in their series of 74, survived six months, whereas 17.5 per cent of their patients with spread to other viscera survived one year or more.

Surgical approach for these hematogenous metastatic pulmonary lesions has been described recently in a few cases. The usual forms of therapy relied on, which include nitrogen mustard, x-ray and androgens, after complete removal of the uterus and adnexae, have given equivocal and generally only palliative results.[1-5, 7]

Maier and Taylor,[7, 8] in 1947, reported a lobectomy for metastatic choriocarcinoma in the right lower lobe followed by a complete hysterectomy and bilateral salpingo-oophorectomy. Radiation of the lungs followed surgery and the patient did well for five years, at which time she developed widespread metastases and died very soon.

An apparent primary tumor of the lung in a 7-month-old girl was removed by pneumonectomy. The child died shortly after surgery and, on post-mortem examination, metastases were found in the opposite lung and the liver (Kay and Reed[9]).

In 1954, Anderson, Bisgard, and Greene[5] reported a case of choriocarcinoma which metastasized to the left lung and was treated with right salpingo-oophorectomy, total hysterectomy, and left pneumonectomy with subsequent advancement of metastases to the right lung. Nitrogen mustard was then used with a rather dramatic response. This patient shows no recurrence of tumor in the remaining lung and the Friedman test is negative.[6]

Spontaneous regression of metastases in the lung has been reported but the question always exists as to whether these are true choriocarcinomas and not chorioadenoma destruens or hydatidiform moles. Novak[3] states, "It is the pathological examination which makes the diagnosis of this lesion and not the clinical history or the hormonal findings." The x-ray diagnosis of pulmonary involvement is quite accurate but must be correlated with the histologic examination of the primary tumor.

Received for publication Dec. 10, 1956.

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Novak[3] speculates that some of the peculiarities of behavior encountered with choriocarcinoma might be linked with the fact that we are dealing with a tumor of one individual, the fetus, growing in the tissues of another, although closely related individual, the mother, making it an implantation type of neoplasm. Immunity may play a part in explaining regression of these tumors inasmuch as trophoblastic tissue is fetal tissue, a foreign protein capable of provoking an antibody response.[1, 10] Cases have also been described where complete disappearance of the original uterine choriocarcinoma has occurred with death of the individual from widespread metastases, as reviewed by Novak and Koff,[11] in 1930, and Novak and Seah,[3] in 1953.

Other vagaries of choriocarcinomatous tumors of the adult female have been reported in the literature. Park and Lees,[12] in their general review of choriocarcinoma, discuss many of these, including those reported cases illustrating delayed metastases or long latency of metastases. They concluded that, "delay of recurrence is rare or does not occur." As a general rule, this is undoubtedly true, as most patients who die of choriocarcinoma, do so within one year.[3] However, the case reported by Maier and Taylor[7, 8] is a clear-cut exception. The following case report, we feel, illustrates not only a delayed recurrence but in addition, a ten-year cure after surgical removal of the metastatic pulmonary recurrence.

CASE REPORT

Mrs. K. B., age 37, was examined at the Buffalo General Hospital on Aug. 31, 1946. She had developed a sudden onset of right lower chest pain on Aug. 7, 1946. The pain was pronounced with each respiration and was exaggerated after reclining or on arising. This phase lasted about two weeks and then gradually improved. She had a slight chronic cough and on occasions produced a small amount of pinkish sputum.

The past history obtained from the Elk County General Hospital, Ridgeway, Pa., was as follows. The patient had been married in 1933. In March of 1935, she had had a dilatation and curettage followed by a partial resection of both ovaries and an appendectomy. This was followed by a tubal pregnancy and a miscarriage. In 1937, she was delivered of a normal child. There was another tubal pregnancy in 1939. On Jan. 20, 1941, she had had a dilatation and curettage and in Jan. 23, 1941, she passed a large piece of decidual tissue and placenta. On Jan. 28, 1941, a supravaginal hysterectomy was performed to stop hemorrhage, adhesions were broken up, and the remainder of the ovaries were left in. Unfortunately, no pathologic reports on any of the tissues are available. There had been no vaginal bleeding from the time of hysterectomy until she was seen at the Buffalo General Hospital on Aug. 31, 1946.

Physical examination at the time of admission was essentially negative except for an area of dullness in the base of the right lung with absent breath sounds. This area was surrounded by a few fine râles. There was a lower midline scar in the abdomen and no nodes were palpable. Pelvic examination was not significant. Laboratory studies revealed on September 3, a urinalysis which was essentially negative; a red blood count, 3.9 million; hemoglobin, 11.2 grams; white blood count, 8,400; bands, 12; filaments, 60; eosinophils, 2; basophils, 1; lymphocytes, 19; monocytes, 6; hematocrit, 40; sedimentation rate, 47; glucose, 102; urea nitrogen, 7. X-ray of the chest on Aug. 31, 1946, showed a . . . "sharply demarcated tumor mass lying in the right chest, posteriorly. The tumor is approximately 4 by 4½ by 4½ inches and the diaphragm is freely moveable below the tumor. The tumor appeared to change shape slightly with the change of position of the patient. This radiographically

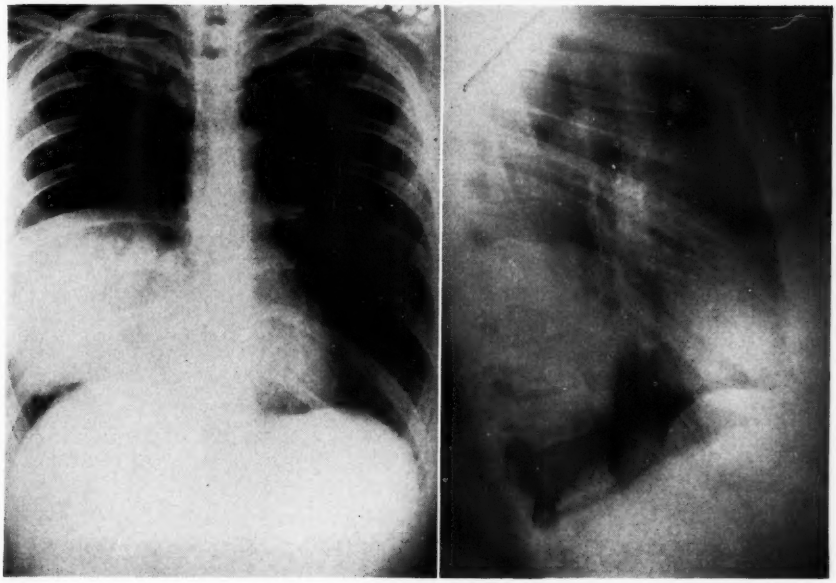

Fig. 1. Fig. 2.

Fig. 1.—Anteroposterior chest film showing tumor in right lower lung field.
Fig. 2.—Lateral chest film showing posterior location of tumor.

Fig. 3.—Horizontal gross section through specimen showing the rounded mass with only a narrow rim of preserved lung tissue remaining.

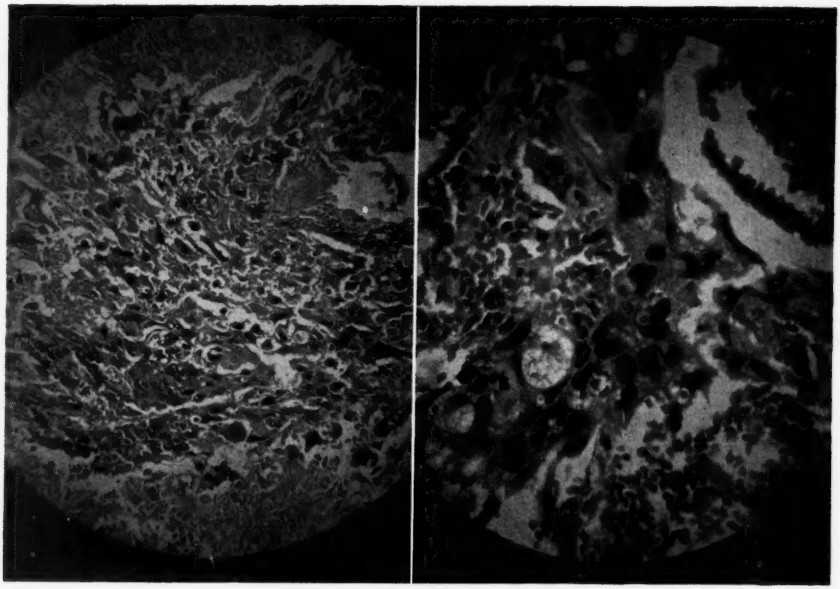

Fig. 4. Fig. 5.

Fig. 4.—Lower power section showing hemorrhagic and necrotic character of the tumor and the numerous bizarre, multinucleated giant cells.

Fig. 5.—High-power section showing the fenestrated syncytial cells lying free and lining vascular spaces.

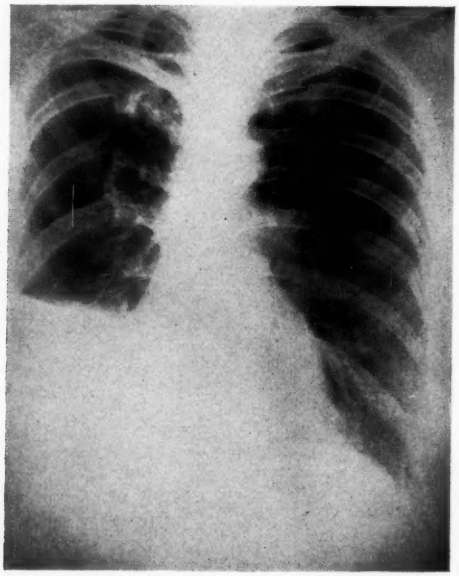

Fig. 6.—Anteroposterior chest film made in February, 1956, ten years after operation showing results of resection and no evidence of recurrence.

has the appearance of a benign tumor, most probably cystic. This could arise from bronchial structure in the pulmonary parenchyma, from the mediastinum, or possibly from the pleura posteriorly.'' (Figs. 1 and 2.)

On Sept. 9, 1946, with a preoperative diagnosis of carcinoma of the lung, a bilobectomy, including the right middle and lower lobes was performed. The patient had an uneventful postoperative course. The gross specimen consisted of resected middle and lower lobe (Fig. 3). Most of the bulk of the lower lobe and a portion of the middle lobe were replaced by a demarcated globular tumor mass. The fresh cut surface was of a grayish and yellow color with large irregular areas of hemorrhage and necrosis. After histologic study, the tumor was erroneously diagnosed as an unusual, immature, anaplastic squamous-cell carcinoma of the lung. Microscopically, there was extensive necrosis and hemorrhage throughout but, where preserved, the pattern was that of a very vascular tumor made up of solid cords and irregular masses of highly anaplastic epithelial cells and numerous multinucleated giant tumor cells. These giant cells had abundant, very eosinophilic staining, fenestrated cytoplasm. The giant cells were commonly found to border or lie free in lakes of blood. No villous structures were noted (Figs. 4 and 5).

On re-examination of the sections, in 1955, during a review of the Hospital cases of lung carcinoma, the true character of the tumor became obvious and the diagnosis of metastatic choriocarcinoma made. From the clinical history, it appeared to be a reasonable assumption that the primary site was a uterine choriocarcinoma. The slides were submitted to Doctor Emil Novak, who kindly reviewed them, concurred in the diagnosis, and accepted the case for the Mathieu Memorial Registry of Chorion-epithelioma.

This patient has been asymptomatic since surgery ten years ago. The chest film is negative and a recent Friedman test was reported negative by her family physician (Fig. 6). There have been no pelvic symptoms.

SUMMARY AND CONCLUSION

A case of delayed metastatic choriocarcinoma of the lung treated solely by bilobectomy has been presented. The patient is alive and well ten years later with no evidence of spread or recurrence. This is a unique occurrence and demonstrates that pulmonary excision alone may have a place in the therapy of this malignant lesion, after the primary tumor and adnexae have been treated.

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SUPERNUMERARY DIAPHRAGM WITH AGENESIS OF UPPER LOBE

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THE literature abounds with cases of defective diaphragmatic development resulting in the many and varied types of hernia. However, a careful search has failed to reveal a single case of two diaphragms developing on one side and hence a brief report of this interesting case seems warranted.

CASE REPORT

The patient was a 4-year-old boy who had been full term at birth, weighing 5 pounds and 8 ounces. After delivery there was some difficulty in initiating respiration and even after breathing did occur, cyanosis persisted. The infant required oxygen for the first twenty-four hours of life.

His mental and physical development seemed normal until at the age of 2 years he began to have intermittent cough and fever. About one year later he suffered pneumonia and subsequently because of persistent nonproductive cough, whooping cough was diagnosed. As he grew older the symptoms increased in severity and the frequency of the attacks of pulmonary infection increased.

The child was admitted to St. Joseph's Hospital, Hamilton, following one of these severe bouts on Nov. 9, 1955, for investigation of possible atelectasis of the right middle lobe, possibly due to foreign body obstruction.

Examination revealed some decreased resonance on the right side with slightly diminished breath sounds in the right mid-chest. X-ray film (Fig. 1) showed some tenting of the right diaphragm and some displacement of the mediastinum to the right. There was no evidence of pneumonitis or atelectasis. Bronchoscopy showed some edema of the right middle lobe orifice, the upper and lower lobe orifices were thought to be normal. Bronchograms failed to reveal any bronchiectasis but an indentation in the lateral wall of the right main bronchus suggested ulceration there to the radiologist. After reviewing these films, it seemed that this indentation represented the beginning of the right upper lobe bronchus and that the middle and lower lobes had actually fanned out their divisions to almost fill the chest cavity (Fig. 2).

Bronchoscopy was repeated by Dr. Love and he reported as follows: "Larynx and trachea normal. . . . There is a marked retraction of the anatomy of the right bronchial tree. . . . The right middle lobe orifice is almost vertical and is clear. The orifice of the right lower lobe is also clear but distorted from normal position. The orifice of the right upper lobe is not visualized but there appears to be a slight indentation where it normally should be. . . . The left bronchial tree is normal."

Two possibilities were considered. It was felt that the most likely diagnosis was recurrent pneumonitis and bouts of respiratory obstruction associated with complete atelectasis of the upper lobe. Against this theory was the fact that numerous radiologic studies from various angles and tomograms failed to reveal any collapsed shrunken upper lobe. The other consideration was agenesis of the right upper lobe but the rarity of this condition plus the fact that it did not explain his symptoms made us feel this was unlikely.

Received for publication Dec. 17, 1956.

On Nov. 30, 1955, the chest was explored through a lateral intercostal incision. The upper lobe was absent. The middle and lower lobes were well developed, free of disease, and somewhat overdistended. The pleural cavity was smaller than usual, the upper part being cut off by a muscular diaphragm. This began posteriorly, curved upward and over the pulmonary artery and bronchus, impinging on them. It then curved downward, became

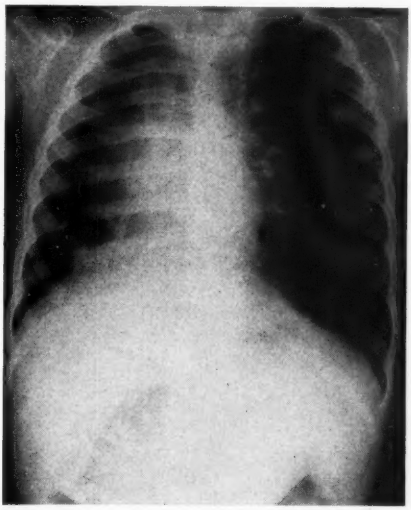

Fig. 1.—Flat plate. Note displacement of mediastinum to right and tenting of diaphragm.

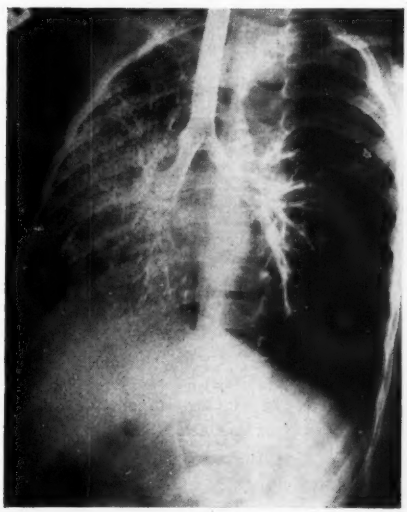

Fig. 2.—Semioblique bronchogram to show stump of bronchus to absent upper lobe.

more tendinous and narrower and passed over the anterolateral aspect of the pericardium to blend with the real diaphragm in front (Fig. 3). The true diaphragm appeared normal and there was no defect present in it.

To relieve the constriction over the bronchus and artery, a triangle of muscle was resected superior to them. Underneath the arch it was then seen that the pulmonary artery was dilated proximally. As the right bronchus was traced upward, a little stump was found projecting where the upper lobe bronchus usually originates. While it was thought that the resected area would relieve the pressure on the hilar structures for the present, it was feared that with further growth the muscular arch might again impinge on the bronchus and artery. Accordingly the tendinous part which curved down over the pericardium was cleared and an area about 2 inches by 1½ inches completely excised so that as the boy becomes taller the two diaphragms will be free to separate and not cause further trouble. Pathologic section of the removed tissue confirmed the diagnosis of tendon and voluntary muscle fibers.

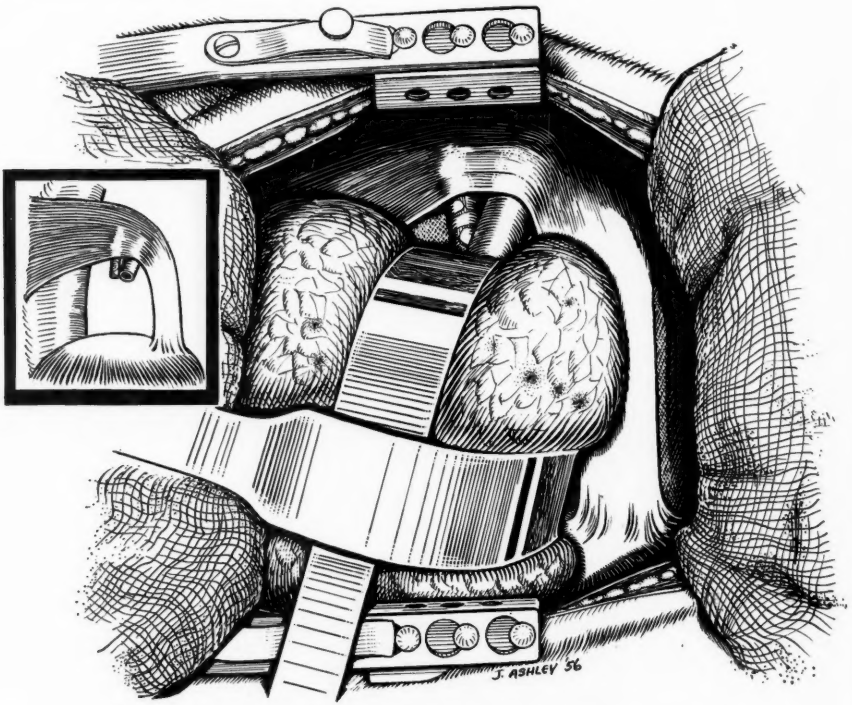

Fig. 3.—Sketch to illustrate accessory diaphragm as seen at operation.

The lobes expanded nicely and the postoperative course was satisfactory; the patient being discharged from hospital on the ninth postoperative day. It is now one year since his operation, and he is thriving, having had no more bouts of pneumonia.

In retrospect, it would appear that once the initial respiratory difficulty at birth was overcome the boy progressed normally until he was about 2 years old, then his increasing length caused the accessory diaphragm to be pulled against the bronchus and, as a result, cough and, later, bouts of pneumonitis began to occur.

DISCUSSION

The diaphragm has a composite origin. The ventral section is derived from the septum transversum. Laterally the pleuroperitoneal membrane normally fuses with the dorsal mesentery and with the mesodermal elements which grow into it from the lateral wall muscle masses. This premuscle tissue is derived principally from the fourth cervical myotome. It seems probable that this mesoderm from the lateral masses, possibly some of that surrounding the right duct of Cuvier, grew across the pleuropericardial opening prematurely and gave rise to this supernumerary diaphragm.

During the fourth week of fetal life the laryngotracheal tube lined with endoderm grows downward and while the cephalic part of the tube forms the larynx, the caudal end forms two lateral outgrowths, the right and left lung buds. At five weeks beginning lobulation is seen as the lung buds grow caudal to the ducts of Cuvier and divide into lobules (three appearing on the right and two on the left). These subdivisions are the early indications of the corresponding lobes of the lung. It probably was about this time that the premature ingrowth from the lateral premuscle mass interposed itself and prevented further development of the right upper lobe, that is, at about the sixth week of fetal life or before.

SUMMARY

1. A case of a supernumerary diaphragm with agenesis of the right upper lobe has been reported in which the accessory diaphragm impinged on the pulmonary artery and bronchus.

2. Following surgery, the symptoms were relieved.

3. A brief discussion of the possible underlying embryology has been presented.

My thanks are due to Dr. E. C. Janes and Dr. E. N. Ballantyne for their helpful suggestions, and to Miss J. Ashley for her drawing.

THE EFFECTS OF AIR EMBOLISM IN THE SYSTEMIC CIRCULATION AND ITS PREVENTION DURING OPEN CARDIAC SURGERY

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THESE studies provide an experimental basis for performing open surgery on the aortic valve. Our experiments were designed to evaluate the effects of systemic air embolism and to develop methods for prevention of air embolism during direct vision surgery on the aortic valve.

METHOD

The effects of air embolism were determined for five sites in the systemic circulation—left atrium, left ventricle, root of the aorta, common carotid artery, and descending thoracic aorta. The amount of air to be injected was usually predetermined by a series of random numbers and was injected through a 22-gauge needle within a period of four seconds or less. Adult dogs were used for all experiments, and they were respired with an electronic respirator if the chest was opened. Every animal was observed until death or sacrifice or until it was apparent that no ill effects had occurred.

In a second group of dogs, aortic valvulotomy under direct vision was performed, and various methods for the prevention of air embolism were then tried. The ascending aorta was clamped throughout the period of valvular exposure and, immediately following closure of the aortic incision with a Beck clamp, all great vessels were ligated and divided, and the heart removed and examined for coronary air embolism. The heart was then placed under water, and the heart chambers and ascending aorta were opened to determine if air was present.

In a third group of dogs, aortic valvulotomy under direct vision during hypothermia was performed to determine the feasibility of this approach to human cases of aortic stenosis.

RESULTS

Small amounts of air in the left atrium are highly lethal. As little as 0.5 c.c. per kilogram usually resulted in coronary air embolism with subsequent cardiac standstill (Table I).

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Supported by the Minnesota Heart Association and the United States Public Health Service (Grant H-1374).
Received for publication Dec. 19, 1956.

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Five-tenths to 1.5 c.c. of air per kilogram injected into the left ventricle was usually fatal (Table I). Even when only 0.5 c.c. per kilogram was injected, coronary air embolism occurred, but the amount of air was sometimes quite small, and one animal was able to move the air over to the venous side without any aid from the surgeon. This dog was the only survivor of this group. Air in the left side of the heart seems to have a predilection for passing into the coronary arteries. With small amounts of air, the coronary artery which is most dependent usually escapes embolization. Right coronary air embolism in the dog appears to be better tolerated than left coronary air embolism.

TABLE I. THE EFFECTS OF SYSTEMIC AIR EMBOLISM ORIGINATING AT DIFFERENT LOCATIONS

NO.	LOCATION	AMOUNT IN C.C./KG.	CORONARY EMBOLISM (%)	CARDIAC STANDSTILL (%)	FIBRILLATION (%)	DEAD (%)
9	l. atrium	0.5-1.5	100	100	66	100
6	l. ventricle	0.5-1.5	100	83	50	83
7	asc. aorta	0.3-1.5	14	14	14	14
4	desc. aorta	8.0-10	50	50	25	100
6	desc. aorta	5.0-7.0	0	0	0	33
2	desc. aorta	3.0-4.0	0	0	0	0

Air in the ascending aorta is tolerated quite well (Table I). Up to 1.5 c.c. per kilogram causes no adverse effects. In all injections, an attempt was made to deliver the air just above the aortic cusps; however, coronary air embolism occurred in only one of 7 dogs. This animal went into ventricular fibrillation following an injection of 1.5 c.c. of air per kilogram and was resuscitated but died 24 hours later. The other 6 dogs were long-term healthy survivors.

Air in the common carotid artery is tolerated much better than air in the left heart. Even 1.0 c.c. per kilogram caused no deaths or cerebral damage in 80 per cent of our dogs (Fig. 1). We observed considerable evidence of cerebral damage for one or two days following the injection of larger amounts of air, but many of these dogs recovered over a period of several days until they appeared to be quite healthy. Gross and microscopic examination of the brain in those animals with severe cerebral dysfunction revealed small focal areas of hemorrhage and necrosis with some cellular infiltration. Whether these experiments can be applied to air embolism in the cerebral circulation of human beings is open to question. The evaluation of slight degrees of cerebral damage in dogs is difficult. Unless our dogs had obvious impairment of sight, hearing, or motor function, or exhibited unusual behavior, it was assumed that they had no cerebral damage. In the human being, finer cerebral deficits would be apparent.

Dogs tolerate relatively large amounts of air in the descending thoracic aorta (Table I). However, if 8 c.c. per kilogram or more is injected, death is likely to occur within a short time. Either coronary air embolism occurs or the right atrium and right ventricle collect so much air that pumping action is impaired. Fig. 2 illustrates the precipitous rise in aortic blood pressure and its gradual fall back to normal following aortic air embolism. A fairly large amount

of air apparently passes through the lung and into the cerebral circulation, for 2 of the survivors in this group had paresis of the hind legs for two days following the experiment.

TABLE II. RESUSCITATION AFTER CORONARY AIR EMBOLISM AND CARDIAC STANDSTILL

NUMBER OF ATTEMPTS	NUMBER IN WHICH VENTRICULAR FIBRILLATION OCCURRED	RESUSCITATION	FAILURE
12	9 (75%)	8 (67%)	4 (33%)

Resuscitation after cardiac standstill due to coronary air embolism was attempted in 12 dogs (Table II). If a large amount of air was present in the left ventricle, it was aspirated with a syringe and needle. The aorta was then

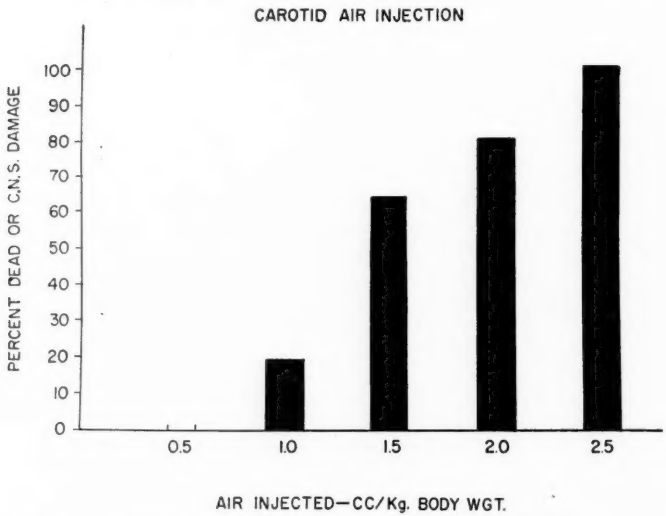

Fig. 1.—This graph represents the results obtained after the rapid injection of air into the common carotid artery of the dog. Each bar except the one at the far right represents an experience with at least 10 dogs.

cross-clamped distal to the subclavian artery, and vigorous manual massage was instituted in an attempt to pump all coronary air over to the venous side of the circulation. Ventricular fibrillation usually occurred, but electrical defibrillation was generally successful after massage had produced a well-oxygenated myocardium. Our success at resuscitation is comparable to that achieved by Geoghegan and Lam.[1, 2]

After aortic valvulotomy under direct vision, it was found that air embolism could be prevented by perfusing the heart through the left atrium and aortotomy incision and releasing the venae cavae for a few moments before closing the aortotomy incision with a clamp. Approximately 50 c.c. of blood, saline, and air were allowed to flow out through the aortic incision before it

was closed. This allows the heart to pump residual air out through the aortic incision without any being forced into the coronary arteries. All other methods which were tried resulted in a high incidence of air embolism (Table III).

TABLE III. PREVENTION OF AIR EMBOLISM AFTER AORTIC VALVULOTOMY UNDER DIRECT VISION

	% AIR EMBOLISM	% CORONARY AIR EMBOLISM
Preferred method—perfuse through atrium and aortotomy and release occlusion before closing aortic incision	0	0
Other methods	86	71

Simulated aortic valvulotomy under direct vision during hypothermia was performed in 13 animals. After cooling in an ice bath to 25° to 30° C., the ascending aorta was exposed through the fourth interspace on the right side.

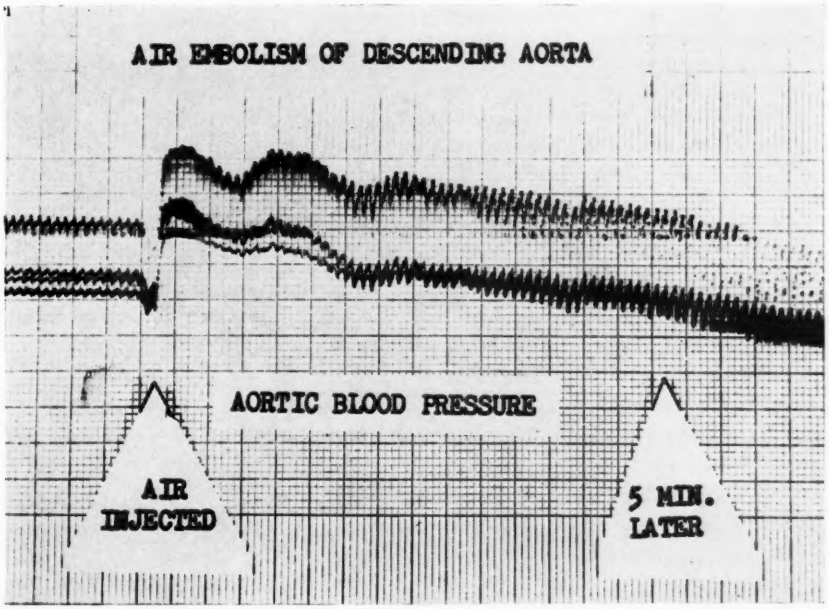

Fig. 2.—Aortic blood pressure following the injection of 4 c.c. of air per kilogram into the descending aorta at the level of the sixth interspace. The transducer was standardized at 4 to 1 with the baseline 5 mm. from the bottom; the aortic blood pressure went from 180/130 to 235/170 following the injection of air but then gradually returned to near normal levels.

The root of the aorta was dissected free of surrounding structures and a Beck aortic clamp used to close off a lip of aorta just distal to the aortic valves. A longitudinal incision was then made in this lip of aorta. After inflow occlusion, the aorta was cross-clamped distal to the longitudinal aortic incision and the Beck clamp released. Blood in the ascending aorta was removed by suction, and the aortic cusps were exposed for five to ten minutes. The heart was then

perfused through a catheter previously placed in the left atrium and through another catheter inserted between the aortic cusps. The venae cavae were then released, and after the heart had pumped approximately 50 c.c. of blood, saline, and air out through the aortic incision, the Beck clamp was used to close the aortic incision. The clamp placed across the aorta was then removed, and the aortic incision closed with a continuous stitch of fine silk. After removal of the Beck clamp, bleeding from the supravalvular incision was usually minimal and could be stopped with slight pressure for a few minutes. Twelve of these dogs were healthy long-term survivors (Table IV). Ventricular fibrillation occurred in 5 dogs, but defibrillation was successful in all 5. Coronary air embolism occurred in only one dog, and the complete procedure outlined above for prevention of air embolism was not used in this case.

TABLE IV. AORTIC VALVULOTOMY UNDER DIRECT VISION DURING HYPOTHERMIA (25 TO 30° C.)

NUMBER	CORONARY AIR EMBOLISM	VENTRICULAR FIBRILLATION	DURATION OF VALVE EXPOSURE	OPERATIVE DEATHS	POSTOP. DEATHS
13	1 (8%)	5 (38%)	5-10 min.	0	1 (8%)

Aortic valvulotomy under direct vision during hypothermia has been introduced by us in human cases for the correction of congenital and acquired aortic stenosis with good results.[3]

SUMMARY

1. The dangers of air embolism occurring at different points in the systemic circulation have been evaluated.

2. Small amounts of air cause no trouble in the systemic circulation unless they are introduced into the left side of the heart, and the resulting coronary air embolism and cardiac standstill can be successfully treated in most cases.

3. After direct vision surgery on the aortic valve, air embolism can be prevented by perfusing the heart with saline through the left atrium and the aortotomy incision and releasing the venae cavae for a few beats before closing the aortic incision.

4. Aortic valvulotomy under direct vision during hypothermia is a safe procedure in the experimental animal and should be a worth-while approach for the surgical treatment of aortic stenosis.

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BENIGN LOCALIZED PLEURAL MESOTHELIOMA

Report of Two Cases

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ALTHOUGH all primary serosal tumors are exceedingly rare, the localized benign pleural form is even more unusual, the exact incidence being unknown since only 17 cases were available in 1953 for a collective review. Furthermore, the association of these lesions with a more or less characteristic pattern of signs and symptoms which are both extra- and intrathoracic is an interesting phenomenon not yet clearly understood. Two typical examples of such tumors treated surgically are presented.

CASE REPORTS

Case 1.—T. A., a 55-year-old Negro man, was admitted to the Veterans Administration Hospital, Houston, Texas, on Sept. 18, 1950, because of the discovery, upon routine chest roentgenographic examination, of a well-circumscribed rounded density in the peripheral portion of the left lung field. There were no symptoms referable to the chest other than a slight, dry, nonproductive cough of one year's duration. He had experienced, particularly in the winter, intermittent pain in both knees and in the upper dorsal vertebrae. The pain was aggravated by exercise. Swelling of the knees had been noted during the winter preceding admission. Past history and review of systems were noncontributory.

Clinical laboratory studies were within normal limits. A chest roentgenogram, on Sept. 19, 1950, revealed a well-circumscribed pulmonary shadow in the peripheral portion of the left mid-lung field (Fig. 1). It was well delineated by surrounding pulmonary parenchyma and the adjacent bony thorax demonstrated no change. The mass was situated in the mid-lung field on lateral projection. To determine the type of pulmonary tumor, diagnostic thoracotomy was recommended. Accordingly, on Oct. 6, 1950, operation was performed through a left standard thoracotomy incision with subperiosteal resection of the fifth rib. Exploration of the left hemithorax revealed a smooth tumor, 5 by 4 cm., attached by a pedicle to the axillary portion of the apical posterior segment of the left upper lobe (Fig. 2). Careful examination of the remaining lung and pleural surfaces revealed no additional pathologic findings. From gross examination and the histologic appearance of a frozen section, it was felt that the lesion was benign. Extirpation was accomplished by a wedge resection of that portion of lung parenchyma which served as attachment for the pedunculated base of the tumor. The patient's postoperative course was uneventful. Chest roentgenograms at the time of his discharge revealed the lungs to be clear and well expanded bilaterally.

Pathology.—The specimen consisted of an ovoid encapsulated mass 6 by 5 by 8.7 cm. (Fig. 3). It was firm and white with red streaking. On gross section a well-developed capsule was evident, within which the tissue was gray-white, firm, and whorled with indistinct lobulation. Several hemorrhagic areas were present near the periphery where

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Received for publication Jan. 24, 1957.

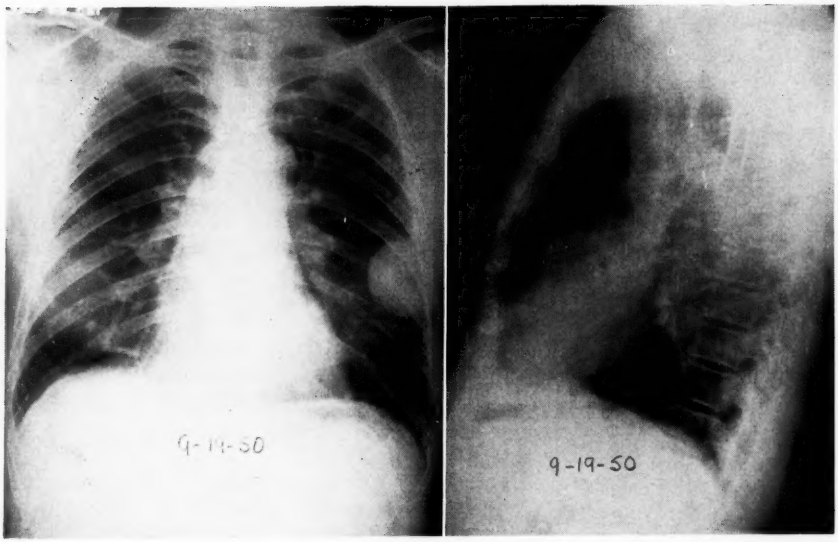

Fig. 1.—Case 1. Preoperative roentgenograms demonstrating a well-circumscribed density in the left lung field.

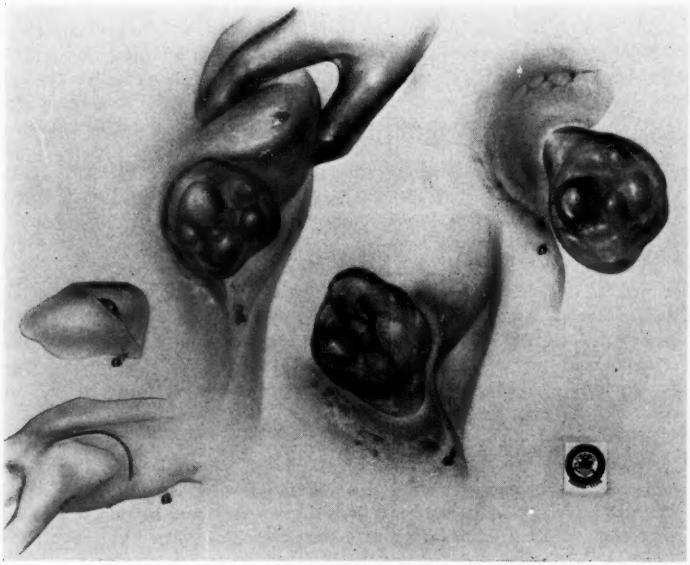

Fig. 2.—Case 1. Composite sketch demonstrating anatomic site of attachment and gross appearance of tumor.

lung tissue was attached. Microscopic study revealed dense fibrous connective tissue with a whorled arrangement (Fig. 4). Many of the fibers were wide and hyalinized. There was mild infiltration of lymphocytes and plasma cells. Along one border a small amount of lung tissue was evident. The capsule was intact and well developed. Diagnosis was mesothelioma of the pleura, benign, fibrous type.

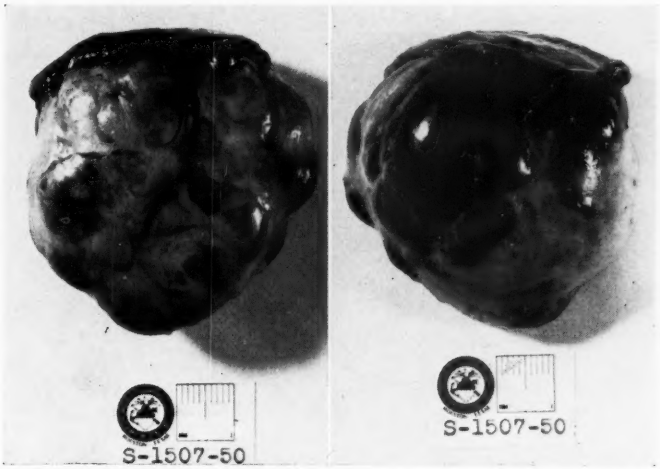

Fig. 3.—Case 1. Photograph of the resected specimen revealing the encapsulated nature of the tumor.

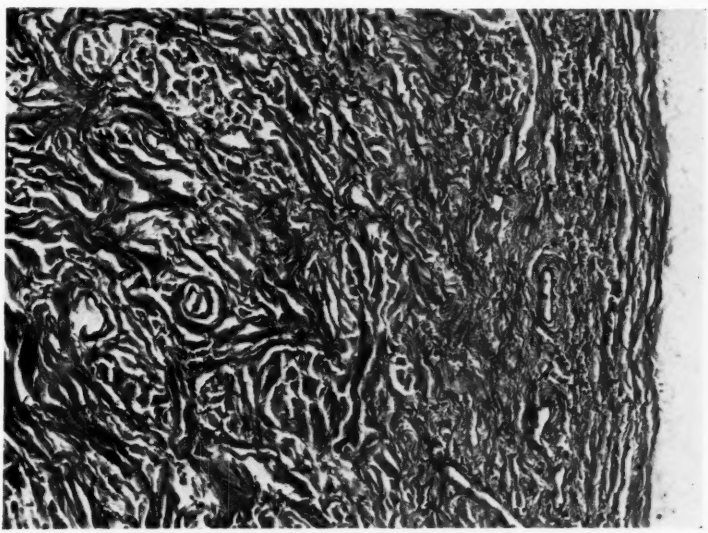

Fig. 4.—Case 1. Histologic appearance of tumor demonstrating capsule and neoplastic connective tissue pattern.

The patient was last examined on Nov. 5, 1954, approximately four years following operation. He was in good health, asymptomatic, and chest roentgenogram revealed both lung fields to be clear. Careful questioning revealed complete disappearance of all joint symptoms.

CASE 2.—E. D., a 55-year-old white man, was admitted to Methodist Hospital, Houston, Texas, on April 17, 1956, complaining of swelling and pain in the ankles. He apparently had been well until four months previous to admission when he developed migratory joint symptoms, primarily of the ankle and feet but also in the elbows, knees, and wrist. Associated with the swelling of the joints had been an increase in local temperature and pain on motion. There were no symptoms referable to the chest other than slight dyspnea on exertion. Hospital admission was prompted by discovery of a mass in the peripheral portion of the left lung upon chest roentgenogram. A routine chest roentgenogram made one year previous to this admission had been reported as revealing no abnormality. Past history was otherwise noncontributory. Significant in the family history was the death of an elder brother from carcinoma of the lung.

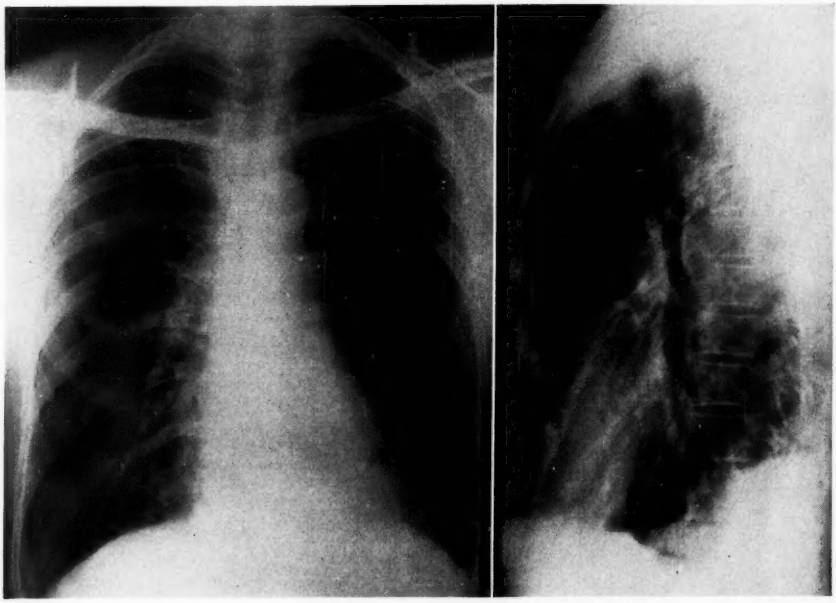

Fig. 5.—Case 2. Chest roentgenograms demonstrating a slightly lobulated mass in the left posterior base.

Physical examination revealed a well-developed and well-nourished man in no apparent distress. There was moderate clubbing of the fingers. The ankle joints were swollen, tender, and painful upon manipulation. Examination of the left chest revealed slightly decreased breath sounds posteriorly. Remainder of the physical examination was noncontributory.

Clinical laboratory studies were within normal limits. A chest roentgenogram on April 18, 1956, revealed a slightly lobulated mass in the left posterior base (Fig. 5). The

tumor appeared to be convex anteriorly with its base against the chest wall. Roentgenographic examination of the ankles failed to demonstrate the usual evidences of pulmonary osteo-arthropathy. A diagnostic thoracotomy was recommended, and, accordingly on April 20, 1956, operation was performed through a left standard thoracotomy incision with resection of the eighth rib. Exploration revealed a pseudo-pedunculated tumor arising from

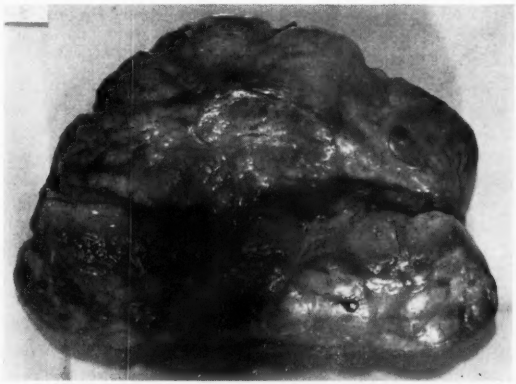

Fig. 6.—Case 2. Photograph of resected tumor.

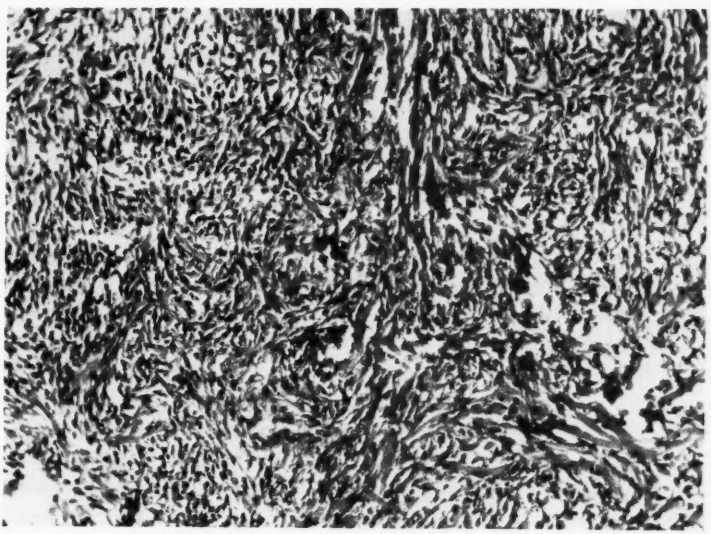

Fig. 7.—Case 2. Histologic appearance of tumor demonstrating distinctive connective tissue pattern.

the posterior aspect of the apical segment of the lower lobe. The 7.5 by 4 by 3 inch tumor was violaceous, firm, slightly nodular, and attached to the peripheral portion of the pulmonary parenchyma by a thin, 4-inch stalk composed of attenuated lung. There was no attachment to the parietal pleura. The remainder of the pleural surfaces, lung

parenchyma, and mediastinum were as usual. Gross appearance and histologic examination suggested that the lesion was benign. Extirpation was accomplished by wedge resection of that portion of the lung parenchyma containing the pedunculated attachment of the tumor. The patient's postoperative course was entirely uneventful and he was discharged on April 27, 1956.

This patient was last seen approximately five months postoperative, at which time he was completely asymptomatic. There had been no subjective joint symptoms and all objective changes had completely subsided. Clubbing of fingers was strikingly improved. A chest roentgenogram revealed no abnormality.

Pathology.—The specimen consisted of a 15 by 9 by 7 cm. tumor with an attached portion of normal-appearing lung (Fig. 6). The external surface was nodular, light brown, and studded with slightly raised gray-white areas somewhat firmer in consistency than the surrounding tumor. Cut surfaces were firm, yellow with gray-white mottling. A definite and intact capsule was evident and surrounding this was a thin layer of compressed pulmonary parenchyma. Histologic examination revealed neoplastic tissue arranged in a distinctive connective tissue pattern (Fig. 7). The individual cells were elongated or spindle shaped with hyperchromatic nuclei and indistinct cytoplasmic borders. Dispersed through the tumor were bands of collagen tissue and numerous thin-walled blood vessels. Masson-trichrome stains demonstrated the previously mentioned collagen connective tissue. Diagnosis was fibrous mesothelioma of the pleura, benign.

COMMENT

Stout[7-10] is credited with having classified tumors arising within the pleural, pericardial, and peritoneal coverings as a single pathologic entity. He in turn attributes the ability to recognize and thus classify these tumors into a single category to the tissue culture work of Murray.[10] She explanted, in vitro, cells of "fibrous" pleural tumors which gave rise to characteristic mesothelial cells. Further study has permitted subdivision into the so-called fibrous type in which spindle cells are arranged in whorled bundles and the glandular type in which cells, which are either spindle shaped or which may resemble epithelial cells, line glandular spaces. In other instances these tumors may reveal both the fibrous and glandular components.

From a gross standpoint, the lesions may be localized, circumscribed, and even pedunculated or may form an extensive surface covering of variable thickness with invasion of underlying visceral and parietal structures. The latter diffuse tumors, not under consideration in this paper, are more commonly encountered than the localized variety. Pleural effusion has been encountered on rare occasions, even in association with local benign lesions, and does not necessarily affect operability. An unusual case reported by Bogardus[2] is said to have shown a central, main tumor with satellite nodules.

The interesting association of arthritic symptoms and clubbing with many of these tumors has been emphasized by Clagett[4] and others.[5, 6, 12] On the basis of clinical observation, Benoit and Aekerman[1] have postulated that these manifestations occur only after the tumor has become sufficiently large to displace an appreciable amount of pulmonary tissue and thereby produce diminution of the volume of respiratory exchange with consequent subclinical hypoxia. Against this is the fact that similar changes do not occur following plombage collapse procedures of fairly large segments of pulmonary

tissue and further by the fact that resection of these focal tumors, with sacrifice of the underlying lobe, may produce relief of symptoms and acute reversal of the clubbing. Further, very small tumors may be associated with arthritic manifestations. Hyaluronic acid extracted from some of these tumors has been suggested as a possible causal agent, but the relationship is not clear. According to Benoit and Ackerman, some of the diffuse tumors found to produce the acid were not associated with clubbing and, conversely, some of the solitary lesions associated with osteo-arthropathy failed to produce the acid.

One interesting case reported by Thomas[11] was that of an elderly woman with joint symptoms relieved by excision of a pleural tumor. After a period of time her joint symptoms recurred; this recurrence, in turn, was followed by manifestations of recurrence of the pleural tumor. At the second operation a pneumonectomy was carried out; this procedure was again followed by re-disappearance of her arthritic manifestations.

Rapid disappearance of extrathoracic symptoms in the 2 cases presented was most striking. The mechanism by which these symptoms were produced was not apparent. Their limited pulmonary attachment and the relatively small amount of pulmonary displacement produced would seem to make chronic hypoxia a most unlikely etiological factor. The presence or absence of hyaluronic acid was unfortunately not determined.

Articles which antedate the work of Stout and Murray are unreliable as source material for incidence, age, sex, and other data because of the varied nomenclature and uncertainty about types of tumor presented. More recent writings probably present a truer picture. Clagett and associates found that of the 24 cases in the files of the Mayo Clinic, 14 were men and 10 were women. Ages varied from 21 to 70 years. In two thirds of these cases the tumor was associated with extrathoracic signs and symptoms including not only the arthritic manifestations referred to above but also chills and fever and, more rarely, cough and chest discomfort. Benoit and Ackerman analyzed 17 cases, 6 of their own and 11 others reported by Stout and Himadi,[9] and Brown and Johnson.[3] In this group the incidence was approximately the same in both men and women. The ages varied between 12 and 64 years and averaged 50 years. Most of their cases were detected by routine roentgenographic examination but on questioning proved actually to be symptomatic, although the symptoms were of such mild intensity that they were dismissed by the patient as insignificant.

Treatment of these lesions is surgical. Occasional mention is made of x-ray therapy in patients who refused operation. No benefit was observed. In the majority of localized tumors, little or no sacrifice of pulmonary tissue is necessary. In some instances, needless sacrifice of such tissue has been carried out because of mistaken interpretation of frozen section examination. Rarely, because of broad attachment, is it necessary to remove a segment or lobe of the underlying lung. Recurrence is fortunately infrequent and in such cases wider re-excision may be carried out successfully.

SUMMARY

The exceedingly rare occurrence of localized benign mesothelioma prompted the report of 2 cases. Both patients experienced migratory joint symptoms as admission complaints and their pulmonary lesions were discovered only on routine chest roentgenograms. Thoracotomy with local excision of the tumor was accomplished in both cases. Rapid disappearance of the extrathoracic symptoms occurred in both patients. The characteristic gross and histologic appearance of a localized benign tumor composed of fibrous tissue cells was demonstrated in each instance. The interesting association of extrathoracic symptoms is discussed and the previously reported cases reviewed.

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Announcements

THE AMERICAN ASSOCIATION FOR THORACIC SURGERY

Notice of Annual Meeting

The Thirty-eighth Annual Meeting of the American Association for Thoracic Surgery will be held May 16, 17, and 18, 1958, in Boston, Massachusetts. Headquarters will be at the Hotel Statler.

Requests for Hotel Reservations

These should be mailed directly to Mr. F. Whitehouse, Front Office Manager, Hotel Statler, Park Square, Boston, Massachusetts. Please mention this Association, the type of accommodation desired, the date, and approximate hour of arrival and departure. If accommodations are desired elsewhere in Boston, please communicate directly with the hotel of your choice.

Thoracic Surgery Forum

The Thoracic Surgery Forum will be continued as a special session at the 1958 meeting. The Forum is primarily for the presentation of short papers on current thoracic research, experimental problems, anatomical studies, and modified or new surgical techniques. The inclusion of any considerable amount of clinical material in these reports makes them unsuited for this session.

Papers at this session will be limited to ten minutes, including the showing of lantern slides or other illustrative material. At the discretion of the President, three minutes may be allowed as the maximum discussion for each paper.

All Thoracic Surgery Forum papers will be published together in one issue of the JOURNAL. Maximum length: 3,000 words without illustrations. If illustrated, an appropriate number of words must be subtracted for each cut used.

Abstracts of Papers

Abstracts of all papers for presentation at the 1958 meeting must be received on or before Dec. 15, 1957, otherwise they will not be considered by the Program Committee.

Abstracts should be labeled "For Thoracic Surgery Forum," or "For Regular Program." They should contain from 200 to 250 words and accurately reflect the content of the completed paper.

Six, repeat, six clearly legible copies of *each* abstract must be sent to Miss Ada Hanvey, Administrative Assistant, The American Association for Thoracic Surgery, 600 South Kingshighway, St. Louis 10, Missouri.

Essayists selected for the program are reminded that papers presented at the meeting *must* be handed to the secretary immediately after their presentation. If they are not ready at that time there is a chance that they will not be published in THE JOURNAL OF THORACIC SURGERY.

Motion Picture Session

Provisions have been made to show a limited number of motion pictures to be selected on a competitive basis. *The films themselves,* together with descriptive material concerning length of presentation, etc., must be received by Dr. Karl P. Klassen, The Ohio State University, Columbus 10, Ohio, before Dec. 15, 1957.

It is planned to run the motion pictures in a smaller room at the same time as the scientific sessions. If the films are well labeled, it will not be necessary for the author to be present for comment.

Applications for Membership

Applications for Associate Membership in the Association must be received by the Membership Committee not later than Dec. 15, 1957, otherwise the application will be deferred for consideration until the 1959 meeting.

Applicants must be sponsored by three Active or Senior Members of the Association. In addition to the signatures on the application form, the sponsors will forward a *separate* letter concerning the applicant directly to:

Dr. Duane Carr
Chairman of the Membership Committee
899 Madison Avenue
Memphis, Tennessee

Sponsors are reminded that *new* letters of recommendation must be forwarded to the Membership Committee should their applicants be held over for reconsideration a *second year.* The new letters of recommendation should also be sent to Dr. Carr, the Chairman of the Membership Committee.